



Annual Progress Report



♦ Fiscal Year 1992 ♦



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13. ABSTRACT (Maximum 200 words) Subject report identifies the research activities conducted at William Beaumont Army Medical Center by investigators who had protocols approved by the Clinical Investigation Committee, the Institutional Review Board, and the Animal Use Committee. This report includes all protocols registered with the Department of Clinical Investigation during FY 1992. All known presentations and publications are also included. The research protocols described were conducted under the provisions of AR 40-38 (Clinical Investigation Program); AR 40-7 (Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Substances); AR 70-25 (Use of Volunteers as Subjects of Research); HSC 40-23 (Management of Clinical Investigation Protocols and Reports); and AR 70-18 (The Use of Animals in DOD Programs).				
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**Headquarters
William Beaumont Army
Medical Center
El Paso, Texas 79920-5001**

**Annual Progress Report
Fiscal Year 1992**

**Clinical Investigation Program
RCS MED-300 (R1)**

**This report was prepared under the direction of
Colonel Manuel Schydlower
Chief, Department of Clinical Investigation
William Beaumont Army Medical Center
El Paso, Texas 79920-5001**

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FORWARD

Clinical investigation activities at WBAMC during FY 92 were distinguished not only by an increase in new and completed protocols but also their high quality. They each represented a continued commitment to excellence in Graduate Medical Education (GME) and research at our MEDCEN by the various residency and fellowship training programs. The support of GME provided by DCI personnel was outstanding in all services: administrative (protocol coordination, editorial assistance, statistical consultation), chemistry, immunology/microbiology, molecular biology, and biological research and human performance/exercise physiology.

Several research projects extended beyond this MEDCEN to include collaborative studies with other institutions from out-of-state, and with Texas Tech Regional Academic Health Center and the University of Texas at El Paso. Extramural funding support of research was again obtained from USAMRDC, USNMRDC, and FACT. Of particular note was the award to DCI by USAMRDC of a major grant for breast cancer research.

During this period, we welcomed the following individuals to our team: MAJ Richard Harris, (Chief, Biological Research Service), CPT William Nauschuetz (Chief, Molecular Biology Service), Specialists Mae Iron Moccasin and Gary Milbradt (Animal Lab Specialists), and Mrs. Vivian Maheu (Editorial Assistant). We will greatly miss colleagues who moved on to other assignments: MAJ Kevin O'Hair, CPT David Smith, Specialists Jasmin Kahn and Bruce Brown, and Ms. Tanya McCollum.

My congratulations and appreciation go to all who contributed so successfully to another year of accomplishment and achievement in the Department of Clinical Investigation. I look forward with enthusiasm to another year of working together. As expressed by the title of this section: Forward!

Manuel Schydlower, M.D.

MANUEL SCHYDLOWER
Colonel, Medical Corps
Chief, Department of Clinical Investigation

UNIT SUMMARY FY 92

Objectives

The Department of Clinical Investigation is responsible for providing the facilities and atmosphere of inquiry necessary to support and stimulate basic and clinical medical investigation within William Beaumont Army Medical Center.

Technical Approach

The Department of Clinical Investigation provides support for staff, fellows and housestaff research projects under the guidelines of the Clinical Investigation Program (AR 40-38); Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances (AR 40-7); Use of Volunteers as Subjects of Research (AR 70-25); Management of Clinical Investigation Protocols and Reports (HSC Reg 40-23); and The Use of Animals in DOD Programs (AR 70-18). Research protocols utilizing laboratory animals also adhere to the guidelines set forth in the "Guide for Laboratory Animal Facilities and Care" (published by the National Academy of Sciences-National Research Council) and the criteria established by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

Research is conducted under protocols approved by the WBAMC Clinical Investigation Committee, Human Use Committee, Radioisotope Committee and Animal Use Committee, as applicable. Committee membership is governed by WBAMC Reg 15-1.

MANPOWER: Listed below is the strength of the Department of Clinical Investigation during FY 92.

<u>Description</u>	<u>Grade</u>	<u>M O S</u>	<u>Br</u>	<u>Req</u>	<u>Auth</u>	<u>Name</u>	<u>Rank</u>
C, Dept Cl Inv	0 6	6 0 P	MC	1	1	Schydlower	0 6
Dir, HP/SCT	0 5	6 0 F	MC	1	1	Weisman	0 5
Immunologist	0 3	6 8 E	MS	1	1	Martig	0 5
Biochemist	0 3	6 8 C	MS	1	1	Smith	0 3
C, Bio Res Svc	0 3	6 4 C	VC	1	1	O'Hair	0 4
Animal Care NCO	E 6	9 1 T	NC	2	1	Williams	E 5
Biol Sci NCO	E 5	0 1 H	NC	1	1		
Biol Sci Asst	E 4	0 1 H		1	1	Delgado	E 4
Animal Care Sp	E 4	9 1 T		1	1	Kahn	E 4
Animal Care Sp	E 3	9 1 T		2	1	Brown	E 3
Supv Res Chem	1 2	1 3 2 0	GS	1	1	Bhattacharyya	1 2
Microbiologist	1 2	4 0 3	GS	1	1	Veit	1 2
Chemist	0 9	1 3 2 0	GS	1	1	Enriquez	0 9
Microbiologist	0 9	4 0 3	GS	1	1	Smiley	0 9
Med Technician	0 7	6 4 5	GS	2	1	Lund	0 7
Med Technician	0 7	6 4 5	GS	2	1	Mana	0 7
Med Technician	0 7	6 4 5	GS	2	1	McIntyre	0 7
Health Tech	0 7	6 4 0	GS	1	1	Revels	0 7
Cl Prot Coord	0 7	3 0 3	GS	1	1	Hineline	0 7
Edit Asst (Typ)	0 7	1 0 8 7	GS	1	1	McCollum	0 7
Sup Clk (Typ)	0 5	2 0 0 5	GS	1	1	Turner	0 4
Anm Caretaker	0 4	5 0 4 8	WG	1	1	Sigholz	0 4
Anm Caretaker	0 1	5 0 4 8	WG	2	1	Burton	0 1

Civilian Personnel with Special Project Funding

Co-Director HP/SCT					Zeballos
Research Nurse	1 1	6 1 0	GS		Chartrand
Exer Physiologist	0 9	4 1 3	GS		Connery
Med Technician	0 6	6 4 5	GS		Badar
Edit Assistant	0 5	1 0 8 7	GS		Peterson

PERSONNEL:

	<u>Required</u>	<u>Authorized</u>	<u>Assigned</u>
Officers	7	5	5
Enlisted	7	5	4
Civilian	18	13	18*

* 5 civilians are funded through special projects

Changes in personnel during FY92:

MAJ Kevin O'Hair replaced by MAJ Richard Harris
 CPT David Smith replaced by CPT William Nauschuetz
 SPC Jasmin Kahn replaced by SPC Mae Iron Moccasin
 SPC Bruce Brown replaced by SPC Gary Milbradt
 Ms Tanya McCollum replaced by Ms Vivian Maheu

GRANTS:

USA Medical Research and Development Command

Intestinal Anastomosis with an Interpositional Absorbable Stent and a Neodymium (Nd):YAG Laser in the Rabbit Model \$15,020

Comparison of Cranial and Iliac Autologous Bone Grafts and Their Effect on the Success Rates of Subsequent Osseointegrated Intra/Extraoral Implant Application in the Miniature Swine. \$2,000

Tracheal Reconstruction with Synthetic Gore-Tex Grafts in the Rabbit Model. \$4,000

Efficacy of Passive Immunization in the Prevention of Infection due to *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* \$54,000

Tracheobronchial Mucins in Health, Disease, and Toxic Exposures \$66,145

Effect of Fibrin Sealant on Skin Graft Inhibition of Wound Contraction in the Porcine Model \$1,000

Effect of Fibrin Sealant on Breaking Strength of Incisional Wounds in the Porcine Model \$2,390

USN Medical Research and Development Command

Joint Navy-Army Human Performance/Sickle Cell Trait Research Project at WBAMC. \$88,000

PROTOCOLS, PRESENTATIONS, PUBLICATIONS:

Protocols	<u>Ongoing</u>	<u>New</u>	<u>Completed</u>	<u>Terminated</u>
FY 90	97	58	37	30
FY 91	112	50	17	18
FY 92	114	67	39	26

	<u>Publications</u>	<u>Presentations</u>
FY 90	62	28
FY 91	48	26
FY 92	40	57

EXPENDITURES:

	<u>FY90</u>	<u>FY91</u>	<u>FY92</u>
Personnel (Civilian)	572,958	549,234	533,655
Consumable Supplies	221,572	233,612	229,484
Capital Equipment	91,748	46,884	131,810
TDY	6,128	8,030	10,762
<u>Printing and Publications</u>	<u>3,019</u>	<u>2,886</u>	<u>2,494</u>
TOTAL	895,425	840,646	908,205
MEDCASE Equipment	62,116	58,000	164,964
Military Pay	<u>538,711</u>	<u>536,758</u>	<u>543,248</u>
TOTAL	1,496,252	1,435,404	1,616,417

PROGRESS FY 92

Biological Research Service

The William Beaumont Biological Research Facility has been fully accredited by the American Association of Laboratory Animal Care (AAALAC) since 1968. Currently, this facility, totaling 7,134 ft², occupies three buildings on the William Beaumont Army Medical Center (WBAMC) complex. The main facility, in Building 7776, contains the surgical suites, radiology, treatment rooms, necropsy, and the majority of the animal holding areas. Building 7774 is utilized as equipment storage plus a new \$66,000, 250 ft², Class 10,000 environmental room used for toxicological and immunological research protocols. The third unit is a new \$10,000, 150 ft², walk-in refrigerator which upgrades and expands the feed storage capabilities for the laboratory animals.

The facility has continued to be extremely active in support of the training and research protocols of WBAMC, combat medical units of Ft. Bliss, regional MEDDACS, and collaborative projects with local civilian medical centers. The biomedical training utilizing animal models is primarily in support of the physician residency programs. Currently, there are 14 ongoing training protocols for physicians encompassing emergency trauma life support, general surgery, laser surgery, laparoscopic techniques, and microsurgery. Two very active and successful training protocols are designed for combat field medics and paramedics in emergency life support procedures. There are a total of 8 active research protocols involving: microsurgery, soft tissue and orthopedic reconstruction, laser surgical techniques, surgical laser applications, pathophysiology of orthopedic stress and bone healing, therapeutic efficacy, environmental toxicology, molecular biology, and immunology.

The Biological Research Service continued with a highly successful collaborative training agreement with the Sierra Medical Center, El Paso, to provide a certification program for physicians, of multiple disciplines, in applications of the surgical laser. Neither WBAMC nor the Sierra Medical Center could unilaterally support this program. However, through collaborative action, over 25 WBAMC physicians will receive certification with tremendous monetary savings to the government.

Equipment upgrades and new acquisitions during FY92 will enhance the training and research support provided to WBAMC. Included is the replacement of metal shelters for the farm animals, the addition of a surgical laparoscopic unit, new surgical lights, and a combination of a Class II biosafety hood and nose-only/whole body inhalation unit for environmental toxicological research.

Major construction plans have been made for expanding the indoor animal holding area of the main facility, design of a bioclean room for immunodeficient rodents, addition of a new surgical suite, and completion of male and female locker/shower rooms.

The Biological Research Facility is looking forward to its triennial on-site inspection by AAALAC during FY93.

Chemistry Section

The chemistry section of DCI is engaged in research projects concerning the effect of retinoic acid (a component of vitamin A) on mucin gene expression in rat and rabbit tracheal epithelial cells in culture exposed to different toxic substances and respiratory drugs, analysis of hemoglobin peptides from humans and animals by high pressure liquid chromatography, and analysis of drug metabolites in children of addicted parents.

We have demonstrated that retinoic acid is one of the most important constituents of the culture medium in which tracheal epithelial cells differentiate and propagate normally. Without retinoic acid, the cells tend not to grow properly, nor do they produce mucin, the secretion of which is the normal function of these cell lines. Ultrastructural examination of the tracheal cells grown in medium containing retinoic acid shows well-established mucociliary epithelium with abundant microvilli and secretory granules. On the other hand, when the cells are grown in medium without retinoic acid, the cells tend to become squamous and lose most microvilli and secretory granules. Hybridization analysis of total RNA isolated from cells grown in medium with retinoic acid indicates the strong expression of mucin gene. The expression becomes weaker in cells grown without the compound. Addition of retinoic acid to the cells grown in medium without retinoic acid results in full expression of mucin gene. Additionally, we have found that retinoic has a protective action against many toxic substances which were injurious to these cell lines. These findings have important implications regarding respiratory diseases such as asthma, chronic bronchitis and cystic fibrosis, where excessive secretion of mucous is a common phenomenon.

We are also involved with two other protocols, entitled, "The effect of bovine TSH on hemoglobin proportions in adult rats", and "Determination of the prevalence of drug affected babies in a military population". The first was prompted by observations that in patients with beta globin chain hemoglobin abnormalities, a high level of fetal hemoglobin is associated with a milder clinical course and that during the postnatal period in humans, there is a switch from fetal hemoglobin (HgbF) to adult hemoglobin (HgbA). A model system has been developed to study the level of hemoglobin components in adult and neonate rats. However, estimation of HgbF level by classical procedures was slow and tedious. We have developed a rapid and sensitive procedure which utilizes high pressure liquid chromatography with a weak cation exchange column to characterize and compare adult and neonate rat hemoglobin components more effectively. The last ongoing protocol is concerned with determination of drug metabolites in meconium of babies that may have been acquired from mothers before delivery. We are now analyzing drug metabolites in meconium by employing gas chromatography/mass spectrometry methods.

Molecular Biology Service

The Department of Clinical Investigation has a Molecular Biology Service which specializes in the development of clinical gene amplification techniques. The section can support the development of procedures to detect pathogenic organisms, oncogenes, and markers for congenital diseases. Polymerase chain reaction (PCR) or isothermic procedures can be used to detect and amplify any known nucleic acid sequences in tissue or body fluids. *In situ* amplification can be done on tissue sections in order to visualize the exact location of the amplified products.

Active protocols include detection of human papillomavirus (HPV) in the urine of sexually active adolescent males; *in situ* amplification of activated HPV oncogenes in adolescent females; diagnosis of tuberculosis using PCR, as well as isothermic amplification of tuberculosis from sputum specimens.

The Molecular Biology Service is currently the only gene amplification facility in the El Paso area, so community projects with the Department of Public Health, Texas Tech Regional Health Science Center, the University of Texas - El Paso, and the local branch of Texas A & M are being developed to rapidly diagnose communicable diseases, including tuberculosis, gastroenteritis and hepatitis.

The equipment used to accomplish these projects includes the Perkin - Elmer 9600 thermal cycler and a 2-column DNA synthesizer.

Immunology and Microbiology Section

Research interests of the Immunology and Microbiology Section have been focused on (1) immunoregulatory subsets of T cells in Bermuda grass allergy, (2) immunoglobulin levels in pediatric patients with chronic otitis media and in patients with hypogammaglobulinemia who are being treated orally with immune gamma globulin, and (3) immune responses to rubella virus. Recently, our section has received two-year funding from USAMRDC for studies of breast cancer. This research program involves the study of growth regulatory factors such as estrogen, epidermal growth factor, transforming growth factors, and insulin-like growth factors, tumor-associated antigens, cellular infiltrates, and the growth dynamics of stromal and breast cancer cells which influence the survival and outgrowth of chemically resistant human breast cancer cells.

It has been hypothesized that suppressor T cells develop as a consequence of immunotherapy and that these suppressor cells are responsible, at least in part, for inhibiting the IgE-mediated release of chemical mediators that characterize the allergic reaction. We have utilized various approaches in an attempt to detect this subset of suppressor T cells in the blood of patients with Bermuda grass allergy who were undergoing immunotherapy. Using a protocol that had been reported to demonstrate the existence of such a population in patients with ragweed allergy, those findings were confirmed in our study population but there was no evidence of suppressor cell activity that was directed toward Bermuda grass allergens. We concluded that the quality and/or quantity of antigen used, as well as the cellular

composition of the population stimulated in vitro, are critical factors in the generation of suppressor cells. It is possible that the allergen preparation that we are using contains a variety of substances which may have counteractive effects that interfere with the development of or mask the expression of the suppressor cells. We are currently attempting to fractionate and purify the relevant allergens by capillary electrophoresis in order to obtain the putative suppressor cell-generating moiety.

It has been hypothesized that chronic otitis media may, in part, be caused by abnormally low levels of certain immunoglobulins or by hypogammaglobulinemia. We are currently accumulating a large number of serum samples from pediatric patients who suffer from chronic otitis media or who are hypogammaglobulinemic and are receiving oral immune globulin. These sera will be tested for IgG, IgE, IgM, IgA, and IgG subclass levels by ELISA to determine whether there is a deficiency in one or several of these immunoglobulin isotypes or subclasses in our two patient populations.

In the past few years, there has been serious concern among communicable disease personnel regarding the high incidence of measles epidemics as well as an increasing incidence of rubella disease in the United States. Recent measles outbreaks in El Paso have provided the opportunity to study military dependent populations of students who received MMR immunizations during the epidemics as well as infant and adult patients who are admitted to the hospital with primary measles disease. We have established an ELISA test to measure total IgG, IgG subclasses, IgA and IgM antibodies to the rubella and measles viruses. Our studies of pre- and post-MMR immunization sera from these children have indicated that approximately 9 to 10% of previously-vaccinated adolescents have very little, if any, durable immunity to measles since, upon revaccination, they experience a four-fold or greater increase in their IgG titers. Whether these individuals are at risk of developing clinical disease upon exposure to wild-type virus is uncertain. However, it is believed that waning or non-durable immunity may be one explanation for the increasing incidence of measles disease in the United States. We have tested several of the same sera for pre- and post-MMR vaccination levels for anti-rubella antibodies to determine whether the same 10% are also deficient in rubella immunity as well. Our results suggest that approximately 90% of these same individuals have little if any durable immunity to rubella since most post-vaccination sera exhibited a 4-fold or greater rise in IgG anti-rubella antibody titers. Current studies are attempting to characterize the nature of the increased antibody titers and to determine whether these are relevant (neutralizing) antibodies.

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Chamales I: Continuity of OB Care in an OB-GYN Training Program. Armed Forces District of the American College of Obstetricians & Gynecologists. Cincinnati, OH, 7-11 Oct 91.

Chamales I: Vaginal Mucositis in Rubeola. Armed Forces District of the American College of Obstetricians & Gynecologists. Cincinnati, OH, 7-11 Oct 91.

Fontenot J: Clomiphene Induced Quintuplets: A Case Report and Review of the Literature. Armed Forces District of the American College of Obstetricians and Gynecologists. Cincinnati, OH, 6-10 Oct 91.

Napolitano P: Preventive Medicine in the Practice of Gynecology (scientific exhibit). Armed Forces District of the American College of Obstetricians and Gynecologists. Cincinnati, OH, 6-10 Oct 91.

Page TE: Comparison of Glucola Versus Karo Syrup in the Performance of the 1 hour Glucose Screening Test. Armed Forces District of the American College of Obstetricians and Gynecologists. Cincinnati, OH, 6-10 Oct 91.

Page TE, Gehlbach D, Harlass FE: Comparison of Error in the Ultrasound Estimation of Fetal Weights by Residents and Perinatologists. Armed Forces District of the American College of Obstetricians & Gynecologists. Cincinnati, OH, 7-11 Oct 91.

Soisson A: Radical Hysterectomy in Obese Patients. Armed Forces District of the American College of Obstetricians & Gynecologists. Cincinnati, OH, 7-11 Oct 91.

Vu K: Operative Laparoscopy for Ectopic Pregnancy in a Residency Program. Armed Forces District of the American College of Obstetricians and Gynecologists. Cincinnati, OH, 6-10 Oct 91.

Wharton G: Carcinoid Tumor of the Appendix Metastatic to a Primary Clear Cell Carcinoma of the Ovary. Armed Forces District of the American College of Obstetricians and Gynecologists. Cincinnati, OH, 6-10 Oct 91.

Wharton G, Hawley-Bowland C: Urinary Stress Incontinence Procedures (scientific exhibit). Armed Forces District of the American College of Obstetricians & Gynecologists. Cincinnati, OH, 7-11 Oct 91.

Pediatrics

Atkinson AW: Attention Deficit Disorders/Hyperactivity - Family and School Issues. 3rd Annual Disabilities Symposium, El Paso Community Coalition of Agencies. El Paso, Texas, 29 Feb 92.

Atkinson AW: Subtypes of Attention Deficits and Their Pharmacological Management. Brain Function & Learning Annual Conference. University of North Texas. 26 Sep 92.

Faucette KJ: The Association Between Trisomy 18 and Wilms Tumor. The First International Conference on Wilms Tumor. The University of New Mexico at Albuquerque, New Mexico, May 1992.

Faucette KJ, Fitzgerald LA, Parker CJ, Rodgers GM: Characterization of the Interactions Between Procoagulant Albumin (PC-AL) and Human Endothelial Cells (EC). American Society of Hematology Meeting. Baltimore, MD, May 92.

Molloy M, Reyna T, Pearl RH, Stafford P: Biliary Dyskinesia in Childhood: Evaluation, Treatment and Outcome in Two Cases (abstract). The 44th SW Surgical Congress Annual Meeting. 26 Apr 92.

Pearl W, Zeballos R, Gregory G, Connery S, Weisman I: The Effects of Hypoxia and Exercise upon the Electrocardiograms of Young Black Men (poster presentation). American Heart Association Meeting. Chicago, IL, 24-25 Jul 92.

Sierra LA, Know MC, Dennis RA, Atkinson AW: An Evaluation of the Association Between Attention Deficit Disorders and Central Auditory Processing Problems (poster presentation; paper finalist). USPS Annual Pediatric Seminar, 23-25 Mar 92.

Wasserman GM: A Novel Approach to Enhancing Immunogenicity and T Cell Specificity Using Preprocessed Antigen to Develop T Lymphocyte Lines to *Plasmodium Vinckei Vinckei* Infection in a Murine Model. Society for Pediatric Research Annual Meeting. Baltimore, MD, 7 May 92.

Wasserman GM: A Novel Approach to Enhancing Immunogenicity and T Cell Specificity Using Preprocessed Antigen to Develop T Lymphocyte Lines to *Plasmodium Vinckei Vinckei* Infection in a Murine Model. Pediatric Triservice Seminar. 23-25 Mar 92. (Presented with permission, in writing, of both the Director, Pediatric Triservice Research Presentations and the President, Society for Pediatric Research).

Wasserman GM: Front Line Medical Operations: Third Armored Cavalry Regiment. Seventh Conference on Military Medicine (Session I: Medical Support to T.O.E. Units). Uniformed Services University of the Health Sciences School of Medicine, 14 Apr 92.

Wasserman GM: Preventive Medicine: U.S. Army (3d Armored Cavalry Regiment). Seventh Conference on Military Medicine (Plenary Session: Preventive Medicine). Uniformed Services University of the Health Sciences School of Medicine, 14 Apr 92.

Wilson B, Faucette, KJ, Parker CJ, Rodgers GM:
Suppression of Endothelial Cell Protein C
Activation by Procoagulant Albumin. American
Federation of Clinical Research Meeting. Carmel,
CA, Feb 92.

Pharmacy Service

Waddell JA: Prescription Refill Pharmacy. Eastern
States Conference for Pharmacy Residents to
Preceptors. Baltimore, MD, 10 Apr 92.

Surgery

Flynn TW, Godges J: Differentiating Facet From
Costovertebral Dysfunction (platform
presentation). 5th International Congress of the
International Federation of Orthopaedic
Manipulative Therapy. Vail, CO, 1-5 Jun 92.

Green R, Weppler CL, McDonough S, Behrman R:
Effect of a Six Week Training Program on Middle
Trapezius Muscle Force and Scapular Position in
Standing Subjects (platform presentation). Texas
Annual Conference. Houston, TX, May 92.

Wynkoop W: The HIV Needlestick-Should
Emergent Management Include Incision and
Debridement? 8th Annual Residents & Fellows
Conference-Southern Orthopaedic Association.
Atlanta, GA, 16-17 Nov 91.

Wynkoop W, Pino W: What is Your Career Risk of
Acquiring HIV Infection? Evaluating the Risk to the
Health Care Worker. 85th Annual Scientific
Assembly, Southern Medical Association. Atlanta,
GA, 16-19 Nov 91.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/17

STATUS: Ongoing

TITLE: Human Tracheal Mucin: Biochemical, Physical and Rheological Studies

START DATE: Mar 86

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Brigitta Manna, John I. Enriquez

KEY WORDS: Tracheal mucin, Human

Study Objective: This protocol is concerned with isolation, purification and characterization of mucin glycoprotein components (mucins) from tracheal secretion of patients with asthma, chronic bronchitis and cystic fibrosis. The glycosylated and nonglycosylated peptides will be isolated, purified and sequenced (peptide portion) after subjecting the purified mucins with different proteolytic enzymes. Antibodies will be developed in rabbits against the nonglycosylated peptides which, in turn, will be used to follow the synthesis and secretion of these macromolecules in a tracheal (or bronchial) culture system. Finally, the viscoelastic properties of purified mucins will be investigated.

Technical Approach:

1. Collect sputum from patients (either male or female, any age) with asthma, chronic bronchitis and cystic fibrosis.
2. Solubilize mucins with water and buffer.
3. Establish the homogeneity of mucin glycoproteins isolated from sputum of patients with asthma, chronic bronchitis, and cystic fibrosis by molecular sieve and ion-exchange chromatography.
4. Isolation and characterization of peptides (or glycopeptides) derived from digestion of mucins with different proteolytic enzymes (Column and HPLC);
5. Amino acid sequence analysis of these peptides by sequenator and cDNA cloning procedure;
6. Raise antibodies in rabbits against these peptides (preferably against nonglycosylated peptides); and finally,
7. Establish a tracheal (or bronchial) culture system to examine the synthesis and control in secretion of these macromolecules by ELISA or radioimmunoassay (RIA) procedures using these antibodies.

In addition to the above, the physical properties of mucins, particularly their interaction (in terms of viscosity) with other serum proteins (such as albumin, immunoglobulin, and fibronectin) will be studied.

Progress: Isolation and characterization of the deglycosylated peptides from human bronchial mucin have been completed. Antibody against the principal peptide (Mr 97,000) has been raised and the antibody was found to react with the deglycosylated peptides of mucins isolated from various sources¹. The carbohydrate portion of the mucins has not been investigated yet. We have now been successful in culturing both rabbit and rat tracheal epithelial cells in serum-free and hormone-supplemented medium and the cells were found to secrete mucins into the culture medium. We are now engaged in studying the control in secretion of mucin by the tracheal epithelial cells in culture.

Reference: 'Bhattacharyya SN; Veit BC; Manna B; Enriquez JI; Walker MP; Khorrami AM; and Kaufman B: Neutral and acidic human tracheobronchial mucin. *Inflammation* 14: 355-373 (1990).

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/16

STATUS: Ongoing

TITLE: Cellular Mechanism of Mucin Secretion: Studies Involving Rat and Rabbit Tracheal Culture System

START DATE: Jan 89

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Brigitta Manna, Maxine Lund, John I. Enriquez

KEY WORDS: Mucin, animal

Study Objective: This proposal is concerned with the isolation and characterization of mucin glycoprotein components (mucin) from secretions of rat and rabbit tracheal epithelial cells in culture and establishing their structural identity with those of the same components from human. The ultimate goal of this proposal is to find an animal model tracheal culture system akin to human where the control mechanism of the secretion of mucins can be studied on the gene level.

Amendment August 1989: In addition to isolation of mucin proteins in the rat and rabbit models, it has become apparent that the isolation and characterization of mucin glycoprotein components from secretions of porcine (swine) tracheal epithelial cells in culture is also necessary. Once the mucin fraction is characterized at the structural level, it can be determined if it is comparable with the same components of human tracheal mucin. The ultimate goal of this proposal is to find an animal model tracheal culture system akin to human where the control mechanism of the secretion of mucins can be studied on the gene level.

Technical Approach: Growth of epithelial cells from rat and rabbit bronchial tissues: Rats and rabbits will be euthanatized and normal appearing tracheal tissues excised aseptically, immersed in cold, sterile L-15 culture medium containing penicillin/streptomycin and transported on ice to the laboratory. Lung tissue is sterilely trimmed away and the bronchus cut into large fragments. Cells are isolated from the human bronchus after an overnight incubation with 0.1% protease solution in minimal essential medium (MEM, Ca++free) done at 4 degrees C. The next day, incubated bronchi are flushed with MEM plus 10% Fetal Calf Serum to remove the digested cells. The cells are washed several times to remove any protease, which is toxic to epithelial cultures. The cell suspension is filtered through a sterile 100U nitrex filter and centrifuged for 10 minutes. Cell pellets are resuspended in cold MEM with 10% FCS and centrifuged again. The cold protease overnight treatment is sufficient to remove most epithelial cells lining the bronchus without much contamination of other cell types from the layer under the basement membrane. After the total cell count is taken, primary cultures are normally initiated by plating $1-2 \times 10^6$ cells per ml per 35mm culture dish. The culture conditions are used for the human bronchial epithelial cells consist of M199 media with D-valine substituted for DL-valine, 10% Fetal Calf Serum, L-glutamine, penicillin/streptomycin, gentamicin, insulin, transferrin, epidermal growth factor, hydrocortisone, cholera toxin, bovine hypothalamus extract, and fungizone. Primary epithelial cultures were then placed in an incubator, with conditions of 37 degrees C., 5% CO₂, and 95% air, and cells allowed to adhere to the culture dish. After 3-4 days incubation, a confluent primary culture of epithelial cells is routinely observed. The cultures received media change and can be used in various studies.

Secretion of mucin and characterization: The synthesis of mucin will be followed by ^3H glucosamine and $^{35}\text{SO}_4$ incorporation. Once the saturation curve is established, radioactive agents will not be used anymore. At the time of maximum secretion, the culture medium will be collected, lyophilized and chromatographed on Sepharose 2B and ECTEOLA column. The purified mucin will be deglycosylated by chemical procedure and the peptide portion will be partially sequenced by sequenator.

Isolation of mucin mRNA and sequencing by cDNA method: The procedure that will follow here is essentially that of Timpte et al. mRNA from tracheal culture will be isolated by guanidine isothiocyanate method followed by oligo(dt)-cellulose chromatography. Construction and screening of the cDNA library utilizing human antiapomucin will be done as described.

Control in secretion of mucin: The synthesis of mucin in epithelial culture will be followed by ^3H glucosamine and $^{35}\text{SO}_4$ incorporation. The control in synthesis will be studies on transcriptional and translational levels using different inhibitory (acetylcysteine and cyclohexamide) and enhancing (pilocarpine) reagents.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Thirty-one rabbits were used this year. Rabbit tracheal epithelial cells were cultured in serum-free and hormone-supplemented medium and found to secrete mucins into the medium. When examined by dot blot analysis, the total RNA isolated from these cells hybridized to an antisense 30-mer oligonucleotide corresponding to a rat intestine mucin peptide sequence, indicating that mucin gene was expressed in these cell lines. Alveoli portion of the lung and liver tissues did not express this gene. Transmission electron microscopy exhibited secretory granules in these cells. Parasympathetic agent (pilocarpine) cholinergic antagonist (atropine), and beta-adrenergic agonist (isoproterenol) alone have little effect on the secretion of mucins. The cholinergic agonist, methacholine, and histamine were found to stimulate production of mucins. Thus, this tracheal culture system can be used as a model system to study upper airway respiratory diseases. Published: In vitro Effects of Drugs on Production of Mucins in Rabbit Tracheal Epithelial Cells Expressing Mucin Gene, Inflammation 16:371-382, 1992.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/37

STATUS: Ongoing

TITLE: Tracheobronchial Mucins in Health, Disease, and Toxic Exposures

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Bruce C. Veit, PhD,

KEY WORDS: *Bronchial mucin*

Study Objective: This proposal has two objectives. One is to prepare a library of mouse monoclonal antibodies against human and rat lung mucin apoprotein to be used as probes for the study of structure and biosynthetic regulation of mucin in tracheal epithelial culture system both at the cellular and DNA level. The other objective is to study the levels and control of transcription and mucin in RNA accumulation in rat tracheal epithelial cells in cultures in response to various noxious agents, like tobacco smoke, ammonia, SO₂ and NO₂, and different drugs.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Animal usage: 892 SD rats. We have made tremendous progress on the protocol. Rat tracheal organ cultures, maintained in a serum-free and hormone-supplemented medium containing retinoic acid had well preserved mucocilliary epithelium and expressed the mucin gene. The other retinoid, retinyl acetate, had a similar effect in inducing mucin gene expression. However, in the absence of retinoids, mucin gene expression was negligible. The presence of fetal bovine serum in the culture medium did not induce the mucin gene expression as strongly as that of retinoids. The oligonucleotide probe showed a positive reaction with total RNA prepared from intestine, but not with the alveolar region of the lung or in the RNA preparation from the liver. Northern hybridization of message showed a size of approximately 7.5Kb. Short-term incubation with pharmacologic agents, methacholine and histamine, resulted in increased mucin gene expression; whereas, compounds like atropine and pilocarpine had little effect. Thus, this culture system has immense possibilities for the study of events that produce different respiratory diseases. The other part of the project, exposure of animals to different pollutants and mechanism of mucin production, will be started soon. The environmental chamber and exposure facilities are already in place now and ready to be activated.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/13

STATUS: Terminated

TITLE: The Effect of L-asparaginase on Pyridoxal-5'-Phosphate Levels in the Rabbit Model

START DATE: Apr 90

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: John I. Enriquez

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Stephen R. Stephenson (MAMC), COL Michael Weir (MAMC)

KEY WORDS: L-asparaginase, Pyridoxal-5'-Phosphate

Study Objective: The objective of this study is to test whether L-asparaginase has an effect on serum pyridoxal-5'-phosphate levels.

Technical Procedure: Following a period of quarantine and observation, the rabbits will be brought to the operating suite in groups of six. Each group of six rabbits will be treated in the following manner:

Rabbit #1, rabbit #2, rabbit #3: 100 u/kg IM L-asparaginase + 10 mg pyridoxine 15 to 30 minutes apart.

Rabbit #4, rabbit #5, rabbit #6: 100 u/kg IM L-asparaginase + saline 15 to 30 minutes apart.

These medications will be repeated daily for five days. On days 1, 3 and 5, blood will be drawn twice from an ear vein for PLP, asparaginine, glutamine, albumin and total protein. Blood will be drawn: one (1) hour before and two (2) hours after medication administration. Blood, for the same analyses, will also be drawn once on day 8 of the following week. Following the last injection and blood draw the rabbits will be returned to the control of the BioResearch Service. In each of two subsequent weeks, six more rabbits per week will be studied similarly. This is a detailed study that hopes to show that there is a specific relationship between the administration of L-asparaginase and the average fall in PLP as well as the asparagine, glutamine, albumin and total protein levels.

Amendment:

a. Experimental Design: Following a period of quarantine and observation, the rabbits will be brought to the treatment room in blocks consisting of a minimum of 4 rabbits (one rabbit per experimental group). Each block of rabbits will be treated in the following manner:

Group A rabbit(s): 100 IU/kg L-asparaginase + 10mg pyridoxine 15 to 30 minutes apart IM.

Group B rabbit(s): 100 IU/kg L-asparaginase + 0.1ml saline 15 to 30 minutes apart IM.

Group C rabbit(s): 10mg pyridoxine + 0.1ml saline 15 to 30 minutes apart IM.

Group D rabbit(s): 0.1ml saline + 0.1ml saline 15 to 30 minutes apart IM.

These medications will be repeated daily for five days. On days 1, 3, and 5, blood will be drawn twice from an ear vein for PLP, asparaginine, glutamine, albumin, total protein, BUN and creatinine. Blood will be drawn one hour before and two hours after medication administration.

Blood for the same analyses will also be drawn once on day 8. Following the last blood draw, the rabbits will be returned to the control of the Biological Research Service. In each of the subsequent weeks, a minimum of one block of rabbits per week will be studied similarly until either enough statistical data is obtained or a total of thirty-six (36) rabbits are utilized. This is a detailed study to attempt to show there is a specific relationship between the administration of L-asparaginase and the average fall in PLP as well as changes in the asparagine, glutamine, albumin, total protein, BUN and creatinine levels.

c. Determination of Number of Animals Required: Thirty-six (36) rabbits will be used. Based upon similar studies, it was determined that 9 animals per group is the minimum number required to generate statistically valid data.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Animal usage: 4 rabbits. Project terminated. Investigators determined further investigation into the premise of finding a correlation between the administration of L-asparaginase and Plasma pyridoxal-5'-phosphate levels is not warranted due to the fact that no clear or significant effect on plasma pyridoxal-5'-phosphate levels due to administration of L-asparaginase was found. No significant changes in the amino acid profiles was noted on the animal subject.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/14

STATUS: Completed

TITLE: Protective Role of Pyridoxine in Gentamicin Nephrotoxicity (in the Rabbit Model)

START DATE: Apr 90

ESTIMATED COMPLETION DATE: Feb 92

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Mohammed A. Nadjem, MC; John I. Enriquez, Sr.; COL Michael Weir, MC

KEY WORDS: Pyridoxine, Gentamycin, Nephrotoxicity

Study Objective: The objective of this study is to test whether pyridoxine has a protective effect on gentamicin nephrotoxicity.

Technical Approach: Following a period of quarantine and observation, the rabbits will be brought to the operating suite in groups of seven. Each group of seven rabbits will be treated in the following manner:

- rabbit #1 - 100 mg pyridoxine (control)
- rabbit #2 - 10 mg/kg gentamicin (IM), 10 mg pyridoxine
- rabbit #3 - 10 mg/kg gentamicin (IM), 100 mg pyridoxine
- rabbit #4 - 10 mg/kg gentamicin (IM), saline
- rabbit #5 - 40 mg/kg gentamicin (IM), 10 mg pyridoxine
- rabbit #6 - 40 mg/kg gentamicin (IM), 100 mg pyridoxine
- rabbit #7 - 40 mg/kg gentamicin (IM), saline

These medications will be repeated every morning for five days. Blood will be drawn from an ear site for PLP, gentamicin and creatinine on days 0, (before injections begin), and two hours after injection on days 1, 3 and 5. Following the last injection and blood draw in the morning, the rabbits will be euthanized in the early afternoon and one kidney from each animal will be recovered for fixation for blinded pathologic interpretation. In each of two subsequent weeks, seven more rabbits per week will be studied similarly. This is a descriptive study that hopes to show that there is a general relationship between the renal pathology and the average fall in PLP, and/or there may be a relationship between pathology and gentamicin blood levels.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Rabbits given 40mg/kg/d of Gentamycin showed mild to moderate renal pathology, predominantly acute tubular necrosis which was prevented by either 10 or 100mg of Vitamin B₆ supplementation. In one rabbit given only 100mg/d of B₆S, moderate renal pathology was observed, although we speculate that this may represent pre-existing renal disease. Further study is needed on the possible nephrotoxicity of high doses of vitamin B₆. Paper published in Veterinary and Human Toxicology, Vol. 34, No. 1, Feb 92, pp 32-36.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/42

STATUS: Completed

TITLE: Risk for Accidental Hot Tap Water Burns

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Bruce Pichoff (TAMC), COL Stephen R. Stephenson (MAMC)

KEY WORDS: Accidental burns, Hot Water

Study Objective: To identify the risk for hot tap water (HTW) injury and assess knowledge about safety limits at our military installation family housing area.

Technical Approach: Sixty family housing units were selected at random for measurement of HTW temperature using both an electronic thermometer and a mechanical thermometer (Oct 88-Mar 89). Household members were asked about their knowledge of HTW safety limits and their awareness of the risk for HTW injury. This study will integrate the epidemiological, retrospective, and decriptive review of the collected data into a final paper.

Progress: This study of 60 randomly selected family housing units at Fort Bliss identified 53 (88%) with HTW temperatures greater than 52°C (125°F) including 44 (73% with HTW temperatures greater than 54°C (130°F). As a result of this study, Fort Bliss developed and implemented safety measures that included setting maximum HTW temperatures in housing units no higher than 49°C (120°F) and instituted periodic checks (twice a year) to ensure safe HTW temperature limits. Paper ready for submission to publication.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/46

STATUS: Completed

TITLE: Adolescent Health Care in the Army Medical System

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Walter Imai

KEY WORDS: Adolescent, Health Care, Military Dependents

Study Objective: To define the primary care needs of the adolescent dependent patient and to examine the care available and needed for this population in the AMEDD system.

Technical Approach: Epidemiologic, retrospective, data on care availability reported by health care facilities in the AMEDD and clinical diagnoses along with demographic data collected by a single provider over a 2-year period will be integrated into a final descriptive paper. Data includes upper age limit for pediatric care, principal diagnoses, patient age and sex, provider specialty, separateness of care facility, consent requirements for care, and chaperonage. Data are not traceable to any individual patient. Data about care availability are not traceable to a particular AMEDD facility. Information derived from the data is described and not compared.

Progress: This study defined the scope of health concerns and availability of care for the common health problems of adolescents in this geographically U.S. Army Medical Department's widespread medical care system of high accessibility. In addition to common respiratory illness, more age-group unique musculoskeletal, psychosocial, dermatologic, gynecologic, and sexuality-related problems are noted. Available care varies by location, with tertiary centers providing more developmental stage appropriate services. These data are useful in planning improved health care delivery to adolescents in the Army medical system as well as other health care systems.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/04

STATUS: Ongoing

TITLE: Activation of T-Cell Subsets in Bermuda Grass Allergy Patients

START DATE: Nov 87

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: Bruce C. Veit PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Rebecca Smiley, BS; Susan McIntyre

KEY WORDS: Allergy, T-cells subsets, Immunoregulation

Study Objective: To determine whether there are detectable changes in numbers and functions of manifestations of Bermuda grass allergy. Since T4+ cells are associated with helper/inducer functions and T8+ cells are associated with cytotoxic/suppressor functions, alterations in the numbers of T4+ or T8+ activated T cells may correlate with changes in the immunoregulatory processes involved in controlling the allergic state. Peripheral blood samples will be obtained from patients during active allergy, immunotherapy, and disease quiescence. Samples will be analyzed by 2-color flow cytometry and by immunohistochemical staining for the distribution of T4+ and T8+ cells and the percentage of activation antigen-positive cells within each of these subsets. T cell subsets will also be analyzed for their ability to increase or suppress the synthesis and/or secretion of IgE. Serum samples from these patients will be analyzed for the presence of soluble IL-2R (circulating IL-2 receptor). These studies should improve our understanding of the immunoregulatory processes involved in the control of IgE-mediated allergic responses.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Further analyses of peripheral blood lymphocytes (PBL) from Bermuda grass allergy (BGA) patients, long-term immunotherapy patients (those receiving BGA therapy) and normal individuals (those without clinical symptoms of allergy) were done by two-color immunofluorescence flow cytometry and tritiated thymidine incorporation following antigen stimulation.

PBLs were incubated for two days in the presence or absence of antigen and then treated with mitomycin C. The putative suppressor cell population was mixed with a responsive population of cells from the same patient together with antigen (Bermuda grass extract) and co-cultured for six days and then pulsed for 24 hours with tritiated thymidine. Aliquots of cells were stained for IL2R expression and subsets of CD8 and CD4 cells to determine percentages of activated cells, suppressor cells and suppressor inducer cells, respectively.

Ragweed activation/suppression was simultaneously studied. Because mitomycin C resulted in across the board activation, mitomycin C-treated cells were incubated alone and followed cytofluorometrically from days 0-6 for expression of CD4 and CD8 subsets and IL2R.

Preliminary data indicates that IL2R positive cells remain viable after mitomycin C treatment, more so than resting cells, and that the suppressor inducer cell population is dramatically reduced, even two days post treatment. These results correlate with the observed enhancing effect of mitomycin C-treated cell populations on the co-cultured cells. Factor production in the supernatants appeared to correlate with the increases in cell activation detected by thymidine incorporation, however, determinations of IL4 and interferon-gamma by

Elisa methodology has not been successful due to lack of sensitivity of the assay. Further development of a more concentrated supernatant, either by increasing cell number in the culture or by lyophilizing the supernatants, as well as optimizing the Elisa detection methodology is underway.

Our results confirmed the observed 30% ragweed immunotherapy short term group demonstrating suppression and lack of demonstrable bermuda suppression in those same patients. Explanation of this phenomenon is still pending and future experimental data is underway, including studies of immunogenicity of the two antigens.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 83/37

STATUS: Ongoing

TITLE: Cardiopulmonary Effects of Stressful Exercise at 4,000 Feet on SCT Individuals (MAJ Becker)

START DATE: Jul 84

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Sick cell trait, Stress, Hypoxia, Exercise

Study Objective: To establish baseline pulmonary function data (spirometry, helium dilution lung volumes, maximum voluntary ventilation L/min (MVV), arterial blood gas analyses (ABG), single breath diffusing capacity DLCO_{SB} (ml/min/mmHg) and steady state diffusing capacity DLCO_{SS} (ml/min/mmHg) (Filly technique) as well as values for the partial pressure of oxygen at 50 saturation (mmHg) (P50) in HgbAS individuals and controls and to determine percent HgbS and percent HgbF in individuals heterozygous for sickle cell trait (HgbAS) at 4000 ft.

To carefully document cardiopulmonary response of individuals identified as having hemoglobin AS during both strenuous incremental and submaximal steady-state exercise at altitude with age, race, sex, smoking, matched non-HgbAS controls.

To correlate observed abnormalities (if any) in parameters of cardiopulmonary performance with levels of HgbS in individuals with sickle cell trait (i.e. are patients with 40 percent of HgbS more likely than controls to experience abnormalities during vigorous exercise. Also, to determine whether HgbF levels may be protective as they are in patients with sickle cell disease.

To determine whether conditioning (repeat studies after six weeks) is operative in modulating cardiopulmonary performance in both SCT individuals and controls.

Conclusive data is not anticipated from this protocol, but a preliminary statement or suggestion may be offered on the important question of occupational restriction of subjects with HgbAS. This is in keeping with the National Academy of Science - National Research Council's Report of 1973.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Addendum (Mar 85): Added testing at 7,500 ft

Progress: 32 subjects were tested. Data collected at simulated 4,000 m (Phase III) is being evaluated.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/38

STATUS: Ongoing

TITLE: Comparison of Physiologic Responses to Prolonged Exercise Simulating Army Field Training in Sickle Cell Trait and Controls (Phase IVa) (Monitor: MAJ Becker)

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: R, Jorge Zeballos, MD; COL John Little, ADA; CPT TW Martin, MC

KEY WORDS: Sickle cell trait, Endurance exercise

Study Objective:

1. To determine if submaximal (50-70% VO₂ max) prolonged treadmill exercise (1 hour 30 minutes) with a final maximum exercise (5 minutes), similar to Army field training conditions, would elicit differences in exercise performance between Sickle Cell Trait (SCT) and control volunteers.
2. To evaluate changes in Percent Sickling (%S) and blood viscosity with prolonged exercise in SCT volunteers and to analyze their relationship to venous oxygen saturation, hydration status and temperature.
3. To assess biochemical and enzymatic changes in blood and urine that would suggest muscle damage (rhabdomyolysis) during prolonged exercise.
4. To compare the effect of prolonged exercise on renal function in SCT and controls.
5. To determine whether subtle pulmonary microcirculatory abnormalities not present at rest would be detected during exercise in SCT compared to controls.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no new enrollments. Narrative unchanged from annual report.

Progress: No new enrollments; data analysis is still underway.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/68

STATUS: Ongoing

TITLE: In Vivo Sickling in Sickle Cell Trait (HbAs): Effect of Hypoxia, Exercise and Red Cell Sampling/Fixation Time (MAJ Becker)

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: R. Jorge Zeballos, MD

KEY WORDS: Sickling, Sickle cell trait, Kinetics

Study Objective: Recent discoveries in Hemoglobin S (HbS) polymerization kinetics make it imperative to re-examine the sickling phenomenon in vivo in order:

1. To corroborate, by using a new, specially designed blood drawing technique, that in vivo sickling is present in the blood of individuals with Sickle Cell Trait.
2. To determine the effect of hypoxia on the magnitude of sickling.
3. To compare the combined effect of hypoxia and exercise on sickling measured in effluent blood from an exercising limb and in arterial blood that has recirculated through the lungs during leg exercise.
4. To determine the effect of red cell sampling/fixation time on the measurement of percent sickling.

Technical Approach: The study will be carried out in the Human Performance/SCT Laboratory at William Beaumont Army Medical Center in El Paso, Texas at an altitude of 1270m and mean barometric pressure of 656mm Hg.

Ten individuals with SCT will be used for this study. All will be between 18 and 28 years of age and will be non-smokers. Volunteers will be obtained from the basic training reception station at Logan Heights, Ft Bliss, Texas similar to previous studies (WBAMC 83/37, WBAMC 88/38). All incoming recruits are screened for SCT with a Sickledex test; positive results will be confirmed by cellulose acetate (pH=8.4) hemoglobin electrophoresis with % HbS determined by quantitative scanning densitometry. Individuals identified as possessing SCT (HbAS) will be asked to participate in the study after an explanation of the protocol, including its purpose, risks and benefits by one of the researchers. Based on past experience, between 30-50% of basic trainees with SCT volunteer to participate. In addition, SCT counseling will be provided by LTC Weisman. This remains important because >70-80% of basic trainees with SCT do not know that they have HbAS or what it means to be positive for HbAS. If the individual with SCT agrees to volunteer in the study, he or (they) will be transported to the SCT lab. Upon arrival, the subjects will read the volunteer agreement and ask any remaining questions. We will explain that they may withdraw from the study at anytime without penalty. If the volunteer withdraws, he will be transported back to his original unit. The NCO will not be informed of the circumstances surrounding the trainee's return. Usually within hours, the former volunteer and the rest of his unit is transferred to a training battalion and a new NCO.

After obtaining informed consent, documented in writing, a physical examination will be performed on each volunteer, and a medical history will be obtained. Baseline EKG, CBC, Urinalysis and SMA-20 will be obtained/checked. If the subject has no contraindication to exercise, he will be accepted into the study. Controls are not necessary for this study.

A 20 gauge venous catheter (3.2 cm length, Quick Cath, Travenol Labs) will be inserted into one of the median antecubital veins of the exercising arm of each volunteer. If an Allen's test reveals a palmar blush within five seconds, a second 20 gauge catheter (Becton, Dickinson) will be placed in the radial artery of the non-exercising arm. Using this technique in over 150 arterial catheter insertions, we have had no ischemic complications; all volunteers have successfully completed basic training. Approximately 30-40% of subjects have experienced minor wrist discomfort which typically resolved within 24 hours without sequelae. No other complications have occurred. Previously approved WBAMC Protocol 88/38 fully discusses the risks of catheterization. The patency of the catheters will be maintained using a heparin flush solution (10 USP unit/ml) intermittently. Blood samples will be drawn anaerobically for blood gas analysis and percent sickling measurements at rest and during exercise.

This is a simplified version of previously approved WBAMC protocols 83/37 ("Cardiopulmonary Effects of Stressful Exercise at Altitude (4000ft) of Individuals with Sick Cell Trait (SCT) with modification to include altitudes of 2300m and 4000m") and WBAMC 87/25 ("Axillary Venous Sickling in Individuals with Sick Cell Trait During Upper Extremity Exercise in a Hypoxic Environment").

The subjects will be studied at rest breathing room air $\text{FIO}_2=21\%$, $\text{PIO}_2=127\text{mmHg}$) and then breathing a hypoxic gas mixture ($\text{FIO}_2=14\%$, $\text{PIO}_2=85\text{mmHg}$) equivalent to 4000m for 15 minutes at rest (before the exercise) and during the exercise tests. The hypoxic gas will be administered via a respiratory gas mask during rest and hand grip exercise and a mouth piece during leg exercise. The inspiratory port of both devices will be connected to a 120L reservoir bag continuously fed from the gas cylinder with the hypoxic gas.

Two types of exercise formats will be used:

a) Hand Grip Exercise: After 15 minutes of breathing the hypoxic gas mixture, the subjects will first perform a maximum rhythmic hand grip exercise at a rate of 60 grips per minute, pulling a weight of 16 pounds from an apparatus, consisting of a hand grip cable, pulley and adjustable weights. The exercise will be performed only with the arm in which the venous catheter has been placed. The duration will be approximately 3 minutes.

b) Leg Exercise: After 15 minutes of breathing the hypoxic gas mixture at rest, the subjects will be exercised on an electronically braked cycle ergometer. The exercise test will consist of two stages of steady state exercise consisting of 5 minute duration each. The first stage will be at 50%, and the second at 75% of the maximum power predicted for each individual. During the cycle exercise test, minute ventilation (VE), oxygen uptake (VO_2), carbon dioxide production (VCO_2), and respiratory exchange ratio (R) will be measured in a breath-by-breath fashion using a computerized system (Medical Graphics Corporation) that integrates flow (pneumotachometer) with the respiratory gases measured continuously in the mouthpiece with a mass spectrometer (Perkin-Elmer). Heart rate (HR) and electrocardiographic changes will be monitored continuously during the exercise tests with an Electrocardiographic System. The arterial blood gas results will be entered in the computer and the physiologic dead space-tidal volume ratio (VD/VT) and the alveolar-arterial oxygen pressure difference [$\text{P}(\text{A}-\text{a})\text{O}_2$] will be calculated.

A short IV extension tube attached to a drawing apparatus will be connected to either the venous or the arterial catheter. The apparatus consists of the following elements: (a) a 3-way stopcock connected in series with (b) a one-way back pressure valve placed between the venous catheter and the port where (c) the syringe with the 1% glutaraldehyde phosphate buffer solution will be connected (a 6cc plastic syringe will hold the glutaraldehyde solution). A (d) plastic safety sleeve will be placed around the plunger and then marked with (e) a red ring. The 1% glutaraldehyde solution is a biological fixative used for fixing blood cells. If this solution is injected into the subject, it could induce serious medical complications. To our knowledge, there is no literature available about the effect of accidental injection of glutaraldehyde into a human being.

The drawing apparatus has been tested for safety by the Clinical Pharmacist of the Hematology/Oncology Service, WBAMC (see attached report). It would appear that this apparatus/technique approaches almost complete freedom from the possibility of accidental

injection of the fixative into the subject; This possibility is even less likely if used by a researcher who is familiar with the system. Another important safety feature is that during the blood sampling, all the maneuvers that are required will be that of pulling the plunger, and never that of pushing or injecting.

Arterial and venous blood samples will be taken at rest breathing room air, at rest breathing the hypoxic gas mixture (14% FIO₂), and at the end of the hand grip and leg exercises, while breathing the hypoxic gas mixture. The blood samples will be drawn and then fixed immediately in the fixative solution (<2sec); immediately thereafter, another blood sample will be collected into a heparinized syringe. This syringe will then be removed from the drawing apparatus, and the blood fixed in glutaraldehyde solution at 30, 60, 180, and 300 second intervals, while being maintained in an anaerobic environment at 37°C. At the end of the Exercise test, the catheters will be removed.

Blood gas analysis will be performed on all samples collected including those used for the measurement of Percent sickling. Oxygen tension, carbon dioxide tension and pH will be measured in an automated blood gas analyzer (IL) and oxygen saturation in a spectrophotometric oximeter (IL CO-Oximeter).

After fixation of the blood samples, slides will be prepared from one to two drops of the glutaraldehyde-red cell suspension and examined under a phase contrast microscope. A thousand cells from random areas of the preparation will be photographed for determination of percent sickling (number of sickled cells per 100 counted). Sickling will be determined independently and in a blind fashion by two observers. A cell will be considered sickled if it is elongated with at least one or two projections or if it is irregularly shaped with an angle and one or more points (21). Ovalocytes, tear drops, echinocytes, and other poikilocytes will be excluded. These criteria for sickling morphology have been adopted and vigorously applied in our lab (22).

An ACLS-qualified physician will monitor the patient's clinical status during the test. Testing will be interrupted if the patient experiences significant discomfort (abdominal pain, muscle cramps) or if a dysrhythmia is noted. A crash cart, supplemental oxygen and defibrillator will be available at all times. In over 150 prior cycle exercise tests with hypoxia we have had no significant complications. We anticipate the catheters will be in place for no longer than two or three hours. After the tests are completed, the catheters will be removed immediately and direct pressure will be applied to the site. A stat vascular surgery consult will be obtained in the unlikely event that a subject develops signs of ischemia.

Semiannual Review: Apr 92 - no new enrollments. Narrative unchanged from annual report.

Progress: No change since FY91 report.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/48

STATUS: Ongoing

TITLE: Practical Value of Hyper-Reactive Airway Testing in the Assessment of Asthma in Army Recruits (Monitor: MAJ Becker)

START DATE: Aug 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: R. Jorge Zeballos MD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Idelle M. Weisman, MC

KEY WORDS: Asthma, AIT, Army recruits, Reactive airway disease, Brochial challenges

Study Objective:

1. To determine whether a screening test for hyperreactive airways "asthma" should be established for individuals who, although having met entry requirements as specified in AR 40-501-2-24d have allergic histories and/or a history of asthma in childhood (HAC), which would appear to increase their likelihood of exercise induced asthma and other asthma related problems during basic training.

2. To determine which of the currently available methodologies, for the diagnostic evaluation of hyperreactive airways, would be most accurate (high sensitivity, high specificity), practical, and cost effective for the screening of potential Army recruits.

3. To modify standard methods for the diagnosis of airway hyperresponsiveness so as to make them more suitable to the Military Entrance Processing Service (MEPS).

4. To propose modification for AR40-501-2-24d based on the results of this study and thereby reduce the number of Existing Prior to Service (EPTS) discharges secondary to asthma.

Technical Approach: All incoming basic trainees at Ft. Bliss will be asked to respond to a questionnaire which will identify the inclusion criteria: (1) history of allergic rhinitis (hay fever), and/or (2) history of allergic dermatologic disorder (i.e., eczema), and/or (3) history of asthma in childhood and (4) normal or border line pulmonary function tests. Service members responding affirmatively to any of the inclusion criteria will be asked to participate in the study.

A physical examination will be performed on each volunteer, and a medical history will be obtained. Baseline EKG, CBC, Total Eosinophil count, and SMA-20 will be obtained/checked.

The study will be conducted on 2 consecutive days in the Human Performance/ Pulmonary Function Labs at WBAMC. On the first day, the exercise induced broncho- constriction test will be performed in the morning, followed by the nebulized distilled water test in the afternoon. On the second day, the hyperventilation with cold air test will be performed in the morning, followed by the nebulized metacholine test in the afternoon. The pulmonary functions at baseline for each test should not differ by more than 5%. The volunteers will be followed during their stay at Ft. Bliss (at least 7-8 weeks) and even longer for those SM's assigned here for AIT. All admissions to a hospital for 48 hours or more, failures to pass the Army Physical Fitness Test, or discharge from the service (especially with a principal diagnosis of asthma) will be carefully documented. A relationship between positivity to hyperreactive airway tests and medical problems related to asthma will be analyzed.

An ACLS-qualified physician will monitor the patient's clinical status during all the testing. Testing will be interrupted if the patient experiences significant chest tightness, wheezing,

shortness of breath, chest pain, or if a dysrhythmia is noted. A crash cart, supplemental oxygen and defibrillator will be available at all times.

Semiannual Review: Apr 92 - no new enrollments. Narrative unchanged from annual report.

Progress: No change since FY91 report.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/75

STATUS: Completed

TITLE: Comparison of Cranial and Iliac Autologous Bone Grafts and their Effect on the Success Rates of Subsequent Osseointegrated Intra/Extraoral Implant Application in the Miniature Swine

START DATE: 2 Feb 90

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: LTC Nathan C. Dickerson

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Michael G. Donovan, DC; MAJ John W. Hellstein, DC

KEY WORDS: Cranial bone graft, onlay bone graft

Study Objective: PHASE I: Design surgical techniques for harvesting bilateral iliac corticocancellous bone grafts, and cranial bone and cranial-facial flap techniques.

(a) Study will provide knowledge for surgical techniques that will minimize morbidity (pain, muscular dysfunction, nerve damage) in swine for future studies.

(b) Phase I study will be performed on one (1) domestic swine prior to bone graft studies (Phase II and Phase III) on more expensive miniature swine.

PHASE II: Compare traditional reconstruction techniques, autologous iliac bone grafts, with autologous cranial bone grafts in maxillofacial reconstruction. Will verify if cranial bone is superior to iliac bone in maxillofacial reconstruction. Facial onlay bone grafts and continuity defect repairs are to be compared.

(a) Will compare rate of revascularization and magnitude of resorption at different time intervals for cranial and iliac bone grafts.

(b) Will evaluate need for donor bone graft to duplicate recipient site.

PHASE III: Will determine degree of osseointegration of pure titanium bone implants in cranial and iliac bone grafts in:

(a) Intraoral continuity defects

(b) Extraoral continuity defects

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Study was completed. Calvarial bone has been reported to be superior to iliac bone for onlay bone grafting due to decreased resorption. This study evaluated the physical, histologic and radiographic characteristics of calvarial and iliac onlay bone grafts in nine Pitman-Moore miniature swine at 2 week, 1, 2, 4, 6, 7, 8, 10 and 12 month intervals. The calvarial onlay grafts had more than a two-fold greater radiographic density than the iliac grafts. Statistical analysis of the mature grafts using the Standard of Estimated Means of the bone graft volumes revealed 85% retention of the calvarial grafts compared to 34% retention of the grafted iliac bone. There was no subjective difference in the rate or degree of

revascularization between the two grafted materials.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/20

STATUS: Ongoing

TITLE: Comparison of Osseointegration of Titanium Implants in Cranial and Iliac Autologous Bone Grafts Stabilized with Immediate Titanium Implant Fixtures in Miniature Swine

START DATE: May 91

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: LTC Nathan C. Dickerson

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Michael G. Donovan

KEY WORDS: Titanium implants, cranial bone grafts, onlay bone grafts

Study Objectives:

1. Examine time interval of osseointegration of titanium implants when placed in immediate bone grafts.
2. Compare the rate of osseointegration, i.e., success rate, of titanium implants in immediate autologous calvarial and iliac bone grafts.
3. Compare the rate of osseointegration, i.e., success rate, between immediate placement of titanium implants in grafted bone to titanium implants in mature bone grafts.
4. Determine the recommended time interval of osseointegration required prior to placement of functional load on implants.

Technical Approach: Six miniature swine will be used for this study. Each animal will serve as its own control by having an implant placed in a non-grafted facial bone site.

Under general anesthesia, each swine will have autologous bone from the outer table of the frontal and parietal bones harvested and a corticancellous bone graft from the iliac crest harvested. Placement of the bone grafts will be to the nasal bones of the swine. The bone grafts will be rigidly fixed utilizing one or more Branemark titanium implant fixtures of 7mm or 10mm lengths.

Four calvarial bone grafts and four iliac bone grafts will be utilized on each animal. The calvarial bone grafts will be on the right side and the iliac bone grafts will be on the left side of the nasal bones.

One swine will be euthanatized at one month, two months, four months, six months, eight months, and twelve months to obtain specimens for histological studies. Twenty-one days prior to scheduled euthanasia and biopsy, the animals will be marked with an I.M. injection of a tetracycline derivative to assess new bone growth in the bone grafts adjacent to the implant fixtures.

Barium sulfate mixed with heparinized formalin will be infused after euthanasia to mark neovascularization in the bone grafts.

Each bone graft site will be physically measured for evidence of bone resorption or growth, and these measurements will be compared with the dimensions of the bone grafts measured at time of initial placement. The titanium implants are of fixed length and will serve as markers for loss or maintenance of the bone graft heights along with the above physical measurements.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal

Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Six animals were used in FY 92. Surgery and necropsy have been completed on eight miniature swine to date. One animal was dropped from the study due to infection in the immediate postoperative stage. Preliminary findings correlate with the preceding protocol #89/75 with greater than 90% retention of the cranial onlay bone grafts compared to less than 30% retention of the iliac onlay bone grafts at one year. Placement of immediate titanium implant fixtures did not affect the retention of the bone grafts. Histological sections and radiographic studies are presently being performed on the bone grafts..

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/37

STATUS: Ongoing

TITLE: Bone-Anchored Craniofacial Prostheses Investigation

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Apr 94

PRINCIPAL INVESTIGATOR: COL Michael G. Donovan

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John Gary, MC

KEY WORDS: Implants, Bone-anchored prostheses

Study Objective:

1. To evaluate the long term retention success rate for titanium implants anchoring craniofacial prostheses.
2. To evaluate the long term stability of the prostheses.

Technical Approach: Patients will be admitted to Ward 6W, and have the routine pre-surgery laboratory studies, to include blood work, x-rays and urinalysis, and any further tests required that would be dictated by their medical history. Appropriate referrals will be given to various medical specialties if indicated. The surgery to implant the prosthesis will be conducted in the operating room. Anesthetic will be given to minimize the pain that is associated with any surgical procedure. The doctor will cut the skin covering the area to be treated and then drill holes in the bones of the face, head, or both. Next, tiny titanium fixtures will be inserted into the holes, the skin will be replaced so that it covers the fixtures, and the skin stitched. The titanium fixtures will be left in place for 3-4 months to allow them to become integrated with the bone. During this time the patient will visit the doctor 2-3 more times so their condition can be monitored.

After 3-4 months, the patient will once again be admitted to the hospital, where they will undergo additional surgery. After the anesthetic is administered, the doctor will again cut the skin covering the area being treated. Some of the tissue under the skin will be removed and the skin will be stitched back together. The doctor will then puncture the skin directly over each implanted titanium fixture and will attach a small skin-penetrating abutment to each fixture. For 3-4 weeks, the treated area will be allowed to heal. During that time the patient will visit their physician 1-3 times so that their condition can be monitored.

After 3-4 weeks, a prosthesis will be made and will be attached to the anchors. After the prosthesis is in place, the patient will continue to visit their physician 3 times during the first year, then twice a year, so that their condition can be monitored, as well as their level of satisfaction.

Progress: Six patients have participated in this study. One patient had the implants placed but does not desire to have them uncovered for attachment of a prosthesis. There were no complications with this patient's care, but it was his personal decision not to proceed. The other five patients have completed their care and are in the follow-up phase as required by the protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/38

STATUS: Ongoing

TITLE: Evaluation of Osseointegration of Immediately Placed Titanium Implant Fixtures in Allogeneic Onlay Bone Graft in Miniature Swine

START DATE: May 92

ESTIMATED COMPLETION DATE: Jan 94

PRINCIPAL INVESTIGATOR: CPT Larry J. Hanson

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Michael Donovan, LTC Nathan Dickerson

KEY WORDS: Titanium implants

Study Objective: To examine if osseointegration of titanium implants occurs in allogeneic onlay bone graft when placed immediately using the concepts of tissue guided regeneration; to examine time interval of osseointegration of titanium implants when placed immediately into allogeneic onlay bone graft using the concepts of tissue guided regeneration; to compare rate of osseointegration, i.e., success rate between placement of titanium implants in allogeneic grafted bone to titanium implants placed in autogenous bone grafts (study #92/20, Comparison of Osseointegration of Titanium Implants in Cranial and Iliac Autologous Bone Grafts Stabilized with Immediate Titanium Implant Fixtures in Miniature Swine); and to determine the recommended time interval of osseointegration required prior to placement of functional load in implants placed in grafted allogeneic bone.

Technical Approach: Fifteen miniature swine will be used for this study. Up to three animals will serve as a source for the allogeneic calvarial and iliac bone grafts to be grafted to the other twelve animals. The long bones from these three animals will serve as a source for Demineralized Bone Powder. The bone will be harvested and then processed by the Department of Anatomy, Medical College of Georgia and the protocol on Appendix A.

Under general anesthesia each of the twelve swine will have allogeneic bone from the frontal and parietal region and allogeneic bone from the iliac crest grafted to the nasal bones, maxilla and mandibular. The allogeneic bone grafts will be augmented with bone morphogenic protein. The bone grafts will be rigidly fixed utilizing one or more Branemark titanium implant fixtures of 10 mm length and Luhr rigid fixation screws.

Five calvarial bone grafts and five iliac bone grafts will be utilized on each animal. The calvarial bone grafts will be on the right side, and the iliac bone grafts will be on the left side of the nasal bones, lateral maxilla, and mandibular ramus.

Two of the calvarial bone grafts and two of the iliac bone grafts will be covered with tissue guided regeneration material from Gore-Tex.

Two swine will be euthanatized at one month, two months, four months, six months, eight months and twelve months to obtain specimens for histological studies.

Barium sulfate mixed with heparinized formalin will be infused after euthanasia to make neovascularization in the bone grafts identifiable radiographically.

Each bone grafts site will be physically measured for evidence of bone resorption or growth, and the measurements will be compared with the dimensions of the bone grafts measured at time of initial placement.

The titanium implants are of fixed length and will serve as markers for loss on maintenance of the bone graft heights as well as the above physical measurements.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Study is awaiting MRDC funding which is expected in Jan 93.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/49

STATUS: Ongoing

TITLE: Evaluation of Alloplastic Material Polytetrafluoroethylene (PTFE) for Reconstruction of Orbital Floor Defects

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: MAJ Larry J. Hanson

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Michael Donovan, LTC Roland Gustafson

KEY WORDS: orbital floor defects

Study Objective: Evaluate the alloplastic graft material Polytetrafluoroethylene (PTFE--GORTEx) for reconstruction of floor of orbit defects in preventing enophthalmos and restoring structural integrity and the histologic compatibility of the PTFE within the orbit over time.

Technical Approach: Ten sheep will be used for this study. Under general anesthesia a surgical defect of uniform size will be made in the orbital floor of each animal. One of the orbital floors will remain unrepaired at each time period to serve as a control for that time period. One millimeter soft tissue patch PTFE will be utilized for the reconstruction of the defect in three of the four orbits per each time period. Measurements to evaluate enophthalmos will be made prior to the making of the floor defect, after the defect is made, after repair, and at euthanasia to evaluate the stability of the reconstruction. Forced duction tests will be performed prior to development of the orbital floor defect, following reconstruction with PTFE, and at euthanasia. Histological sections through the orbital floor will be evaluated for signs of inflammation and foreign body reaction. Histologic evaluation of the structural integrity of the graft material will also be evaluated. Histological evaluation of the adjacent sinus mucosa, regional lymph nodes, and control lymph nodes from the lower extremity will be evaluated. Sinus mucosa will be biopsied for signs of infection/inflammation at the time of the original surgery.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Once the sheep have been procured and arrive, the study will commence.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/48

STATUS: Ongoing

TITLE: Intradermal Hepatitis B Vaccination in Patients with Chronic Renal Insufficiency and End Stage Renal Disease (Monitor: LTC Lane)

START DATE: Jun 92

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: MAJ Jeffrey R. Abrams

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Gregory Pisel

KEY WORDS: hepatitis vaccination, renal failure

Study Objective: To demonstrate the efficacy of intradermal administration of hepatitis vaccine in hemodialysis patients.

Technical Approach: This is a prospective observational study. The investigators intend to demonstrate the efficacy of such a strategy in our dialysis patients and in patients with severe chronic insufficiency. Six hemodialysis patients (one a prior non-responder), and several patients (approx. 6-10) with chronic renal insufficiency will be vaccinated with intradermal Recombivax (recombinant vaccine) every other week and monitored for delayed type hypersensitivity (DTH) reactions. Vaccination will continue until the patient receives 5 doses or develops a DTH reaction. The literature cites no significant adverse reactions to such a regimen except for the possibility of persistent induration and discoloration at the site of inoculation. Bleeding at the site of inoculation might occur as a consequence of recent anticoagulation (dose would be given following the dialysis procedure). NOTE: Study changed to More than Minimal Risk with semiannual review and medical monitor assigned Jul 92.

Progress: Eight patients with end stage renal disease have been enrolled to date. Four patients completed the series (3 have converted; 1 expired soon after receiving the complete series of 5 injections without antibody conversion). One patient received a kidney transplant after his second injection which may confound results; however, we will continue to immunize him and monitor antibody levels as planned. Three more patients are continuing in the protocol. We plan to recruit more patients with ESRD to maintain a more homogeneous patient population, but if unable to get the planned number of participant, will enroll patients with severe CRF/near ESRD. One patient was counseled to enroll, a consent form signed and H&P performed. He received a single injection of Heptavax but subsequently, the lab report was corrected to antibody positivity. He was removed from the study. No adverse outcome occurred in this patient or any other.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/22

STATUS: Ongoing

TITLE: Influence of Endogenous and Exogenous Lipids on Pulse and CO-oximetry Measurements (Monitor: LTC Lane)

START DATE: Mar 92

ESTIMATED COMPLETION DATE: Apr 93

PRINCIPAL INVESTIGATOR: MAJ Gregory Becker

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Thien Do, MAJ Ray C. Johnson, CPT Gregory Mock

KEY WORDS: lipids, intralipid, oximetry

Study Objective: To determine if intralipid infusion will influence CO-oximetry variables in critically ill patients; to determine if intralipid infusion will influence pulse oximetry in critically ill patients; to assess if endogenous hyperlipidemia is associated with artifactual changes in CO-oximetry measurements or pulse oximetry; and to determine if both four and six wavelength whole blood spectrophotometry is prone to lipid induced artifact.

Technical Approach: Twenty patients will be recruited as controls by the investigators for this study and informed consent will be obtained. Demographic data, a medical problem list, and medications will be recorded on the attached data sheet after a brief interview and chart review. Venipuncture will be performed by one of the investigators and specimens will be sent to the clinical lab with an accompanying requisition slip for a Lipid 2 profile, CBC, and Liver profile. Patients will not be used as controls if there are one or more of any exclusion criteria present (noted elsewhere) or if the lipid profile reveals a diagnosis of hyperlipoproteinemia. Radial artery puncture will be performed by one the investigators or a credentialed Pulmonary Service technician. Both a room air arterial blood gas analysis will be run and recorded on this sample as well as oximetry variables on both the IL-282 CO-oximeter and Radiometer OSM3 hemoximeter. The patient's room air pulse oximetry reading on a single pulse oximeter unit will be performed and recorded.

Forty consecutive patients in the intensive care units who are to receive Intralipid infusion will be recruited by the investigators and informed consent will be obtained from the patient or his/her next of kin or legal guardian. Exclusion criteria are listed elsewhere in this protocol. Demographic data, a medical problem list, and medications will be recorded on the attached data sheet after a brief interview and chart review. Immediately before an 8 hour infusion of Intralipid, baseline specimens will be obtained by the investigators (via venipuncture or aspiration of a specimen from an indwelling line) for a Lipid 2 profile, CBC, and liver profile; and a radial artery puncture (or aspiration of a sample from an indwelling arterial line) will be performed by the investigators and handcarried to Respiratory Care and the Pulmonary Lab for ABG analysis and whole blood oximetry on both the IL-282 CO-oximeter and OSM3 hemoximeter. F_iO_2 will be recorded on the data sheet. Pulse oximetry using the same unit as in controls will be measured and recorded as well. All specimens and measurements except the baseline liver panel will be repeated midway during the infusion, immediately after, and the following morning. A liver panel will be obtained in order to assess whether those patients with liver dysfunction (who may not metabolize lipid particles as rapidly), if any, are more prone to lipid induced artifact in any of the measurements made.

Forty consecutive patients who have a new diagnosis of or who are about to undergo initial therapy for hyperlipo- proteinemia will be recruited by the investigators from the Internal

Medicine Clinic and other ambulatory settings and informed consent will be obtained. Demographic data, a medical problem list, and medications will be recorded on the attached data sheet after a brief interview and chart review. Venipuncture will be performed by one of the investigators and specimens will be sent to the clinical lab with an accompanying requisition slip for a Lipid 2 profile, CBC, and liver profile. Radial artery puncture will be performed by one of the investigators or a credentialed Pulmonary Service technician. A room air arterial blood gas analysis will be run and recorded on this sample as well as oximetry variables on both the IL-282 CO-oximeter and Radiometer OSM3 hemoximeter. The patient's room air pulse oximetry reading on the same single pulse oximeter unit will be performed and recorded. All specimens and measurements will be repeated and recorded after telephonic arrangements are made for a repeat testing date after about 3 months of therapy.

Statistical analysis of the data using a SPSS/PC+ statistical program will be performed. Specific analysis will include, but not be limited to, the assessment of statistically significant differences in: (a) oximetry variables measured at the same time on the IL-282 vs. OSM3 hemoximeter in patients and controls; (b) determination of Hgb concentration by oximetry (4 or 6 wavelength) vs the hemoglobinometry method used in the clinical lab by Coulter Counter; (c) oximetry variables, blood gases, lipid levels, CBC values, or pulse oximetry measurements made before, during and after Intralipid infusion in critically ill patients; (d) oximetry variables and pulse oximetry in controls vs. patients with untreated hyperlipidemia; and (e) oximetry variables, blood gases, lipid levels, CBC values, or pulse oximetry measurements pre and post dietary and/or pharmacologic therapy for patients with endogenous hyperlipidemia.

Amended Apr 92: Study changed to More than Minimal Risk and amended to require informed consent from all patients.

Progress: A total of 9 subjects have been enrolled. Six patients in an ICU had whole blood oximetry monitored during intralipid infusion. Only one subject has shown significant change in variables (artifactual increase in methemoglobin). The investigators believe previously reported animal/in vitro studies may have overstated the problem that intralipid infusion in clinically administered doses does not appear to have a marked effect on the oximetric determination of Hgb species. Three subjects in endogenous hyperlipemia had baseline determinations. Follow-up studies have not been done and conclusion cannot be made at this time.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/08

STATUS: Ongoing

TITLE: A Study Investigating Safety and Duration of Effect of Isosorbide-5-Mononitrate in a Controlled-Release Formulation in Patients with Stable Effort Angina Pectoris (Monitor: MAJ Johnson)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: MAJ Roger J. Belbel

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL William Pearl, MAJ Timothy W. Martin

KEY WORDS: Isosorbide-5-Mononitrate

Study Objective: To determine the safety and effectiveness of Isosorbide-5-Mononitrate controlled release formulation. This is a long-acting medication designed to keep the coronary arteries open. It is taken by mouth once a day. This is the final stage of testing a new medication before it becomes available for general use. In previous testing in humans, it has been found to be both safe and effective.

Technical Approach: Twenty adult volunteers will be enrolled. All will have stable effort angina pectoris. Subject will undergo a medical history, physical examination, and laboratory screen including chest x-ray, electrocardiogram, urinalysis, and blood chemistries. Two treadmill exercise tolerance tests will be performed at five to ten day intervals before beginning medication with Isosorbide-5-Mononitrate. The patients will then be randomly divided into three groups. They will either take a placebo, 60 mg of Isosorbide-5-Mononitrate per day or 120 mg of Isosorbide-5-Mononitrate daily. Neither the patient nor the investigator will know which patients are taking which medications. Upon commencing the medication, graded exercise tolerance tests will be performed on the 14th, 28th, and 42nd days. At the time of each of these treadmill tests, the patient will undergo a physical examination including determination of weight, heart rate, and blood pressure. A resting electrocardiogram will also be taken at the time. The entire protocol is expected to accrue approximately 150 patients. It is estimated that William Beaumont will accrue 20 patients.

Semiannual Review: Apr 92 - project due to begin in May.

Progress: Four patients have been enrolled in the protocol. Of these, 1 was a protocol violation, 2 successfully completed the study (1 continued for further cardiac followup), and 1 was dropped from the protocol for being a non-nitrate responder. Upwards of 100 records have been screened for entrance and some 25 patients treadmilled for pre-entrance qualification. There are no ongoing studies at this time, however, we are in the process of considering several potential patients.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/07

STATUS: Completed

TITLE: Apache II Score and Other Prognostic Factors in Determining the Outcome of Patients with GI Bleed Diagnosis

START DATE: Nov 91

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Thein Do

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC William N. Lane, CPT Carlos Jimenez

KEY WORDS: prognostic factors

Study Objective: To see if readily available admission data such as PT, PTT, serum albumin, platelet count, toxic drugs, serum bilirubin, and medical co-morbidities have any predictive power toward patient outcomes and, if so, can they form a strong algorithm with high predictive value which can estimate the mortality risk for each patient admitted to the hospital with GI bleed as part of multiple principle admission diagnoses or in a smaller subset of patients with GI bleed as the main admission diagnosis. From these data, one can separate the population with the greatest mortality risks who would potentially benefit the most from the high level medical care offered in an MICU setting.

Other determinations included: 1) whether admission to the ward or MICU will change the outcome of patients with similar prognostic factors & APACHE II scores; 2) which resuscitative modalities or diagnostic methods have the greatest influence on patient outcome; 3) how predictive is our calculated mortality risk when compared to the actual mortality rate; and 4) determine if the above admission data can predict which patients will require aggressive hemodynamic monitoring, inotropic support in the ICU setting. The ultimate goal is to form a reporting system reliable enough to ultimately point out areas of weakness so improvement can be made.

Technical Approach: Review charts of all patients admitted to WBAMC medical ward or ICU from 12/89 to 8/90 with GI bleed as part of their admission diagnoses and collect APACHE II SCORES, co-morbidities, pertinent laboratory data, and diagnostic modalities done within 24 and 72 hours of admission. The outcome will be described as survived if patient was discharged from hospital to home in stable condition (no patients sent home to die with terminal condition) and as death if patient expired from any cause while in the hospital. From these data, a mortality risk for a given algorithm score can be calculated. This preliminary data will then be validated by comparing it to another set of patients admitted between 8/90 to 4/91 to see if the predicted mortality risk correlates with the actual mortality risk. This mortality prediction system will be further refined by using the combined data set of patients admitted from 12/89 to 4/91. Attempts to compare patients with similar predicted mortality risks treated on the ward versus those treated in MICU will also be made to see if patient outcome is altered with different levels of care (if sufficient number of patients are available). Intuitively, this should be true for GI Bleed and all other medical conditions.

Amendment (Jan 92): Expanded data base to include period of Jan-Dec 91 and added CPT Jimenez as an associate investigator.

Progress: The study indicated it is possible to quickly and accurately predict the mortality rate of patients with GI bleeding in an emergency room setting with data derived from the APACHE II score and serum total bilirubin. This approach offered advantages over APACHE II alone and the newer APACHE III. The statistically significant improvement in outcome prediction seen with serum total bilirubin is probably due to its value as a strong indicator of liver dysfunction and its strong association to life-threatening bleeding varices. Future study may include examining the possibility that the predicted mortality can improve hospital resource allocation by matching the patient's prognosis with the appropriate level of medical care (i.e., intensive care unit, step down unit, or medical ward). Scheduled for presentation in Nov 92 at the Army American College of Physicians meeting.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/61

STATUS: Ongoing

TITLE: Management of the Terminally Ill Patient in an Army Teaching Hospital

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: CPT Carlos E. Jimenez

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL William Lane, CPT Thien Do

KEY WORDS: terminally ill

Study Objective: (1) To examine the age, gender, race, history of end organ/malignancy diseases and underlying cause of death of the involved individuals. We will calculate averages and percentages when indicated to demonstrate a pattern/majority. (2) To determine if a DNR status was ever discussed (patient, family, both or neither) and decided during the hospitalization (first 24 hours and after). Also, we will determine if the patient had a living will prior to or during the hospitalization. (3) To examine hospital course in terms of duration, procedures performed, limitation of care, entrance into the seriously ill list, ICU admissions, and autopsies performed. (4) To determine how many of the patients were followed by any of the sub-specialty clinics in the Department of Medicine. (5) To determine any possible relationship among the DNR status (first 24 hrs and after 24 hrs) vs. invasive procedures, admission to the ICU, hospital days, limitation of care, and end organ disease/malignancy.

Technical Approach: This will be a retrospective chart review to include treatment master file, death certificate, autopsy report, narrative summary, admission history and physical and progress notes. The study will include about 150 patients who died during the study period. A specific data collection sheet will be created to retrieve the pertinent information in an organized fashion. Patient name and social security will not be presented in order to protect patient's confidentiality.

Progress: Data collection is complete with 172 charts reviewed. Analysis underway to develop conclusions. Scheduled for presentation in Nov 92 at the Army American College of Physicians meeting.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/16

STATUS: Ongoing

TITLE: Incidence and Clinical Significance of Adrenal Hemorrhage in Septic Shock (Monitor: LTC Lane)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: MAJ Ray Johnson

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Greg Becker, CPT Robert Wolfgang, CPT Thomas P. Baker

KEY WORDS: adrenal hemorrhage, septic shock

Study Objective: To determine the relationship between acute adrenal hemorrhage, adrenal insufficiency and clinical outcome.

Technical Approach: Those subjects admitted to the critical care units who are eligible for entry will have baseline serum cortisol levels obtained followed by stimulatory assessment of the adrenals with a short cosyntropin stimulation test as previously described. The septic state will be treated with therapeutic modalities as deemed necessary by the primary care provider. Those subjects surviving the septic episode should undergo abdominal CT scanning with examination of the adrenals for evidence of hemorrhage. Non-survivors should undergo autopsy with adrenal examination for evidence of hemorrhage.

Amendment (May 92): Protocol upgraded to More than Minimal Risk and amended to require consent from all patients.

Progress: No patients have been enrolled to date. Patients meeting entry criteria cannot provide informed consent. HSC does not allow use of surrogates in this study, therefore, enrollment is difficult.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/65

STATUS: Completed

TITLE: Emergency Use of Fludarabine in Patient R.G.

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: COL Raymond Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Fludarabine

Study Objective: To treat patient with Chronic Lymphocytic Leukemia (CLL).

Technical Approach: Fludarabine (IND #312887) will be dispensed IAW drug company protocol.

Progress: Protocol completed. Patient is still taking the drug and doing well with no unmanageable side effects. FDA approval granted this year.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/54

STATUS: Ongoing

TITLE: Prospective Evaluation of Coccidioidomycosis in Human Immunodeficiency Virus-Infected Individuals Living in an Endemic Area

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Aug 96

PRINCIPAL INVESTIGATOR: Lynn McNicol

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Naomi Aronson, MC; PA Gregory Martin

KEY WORDS: Coccidioidomycosis, Human Immunodeficiency Virus

Study Objective: To demonstrate whether coccidiomycosis seen in HIV patients is reactivation disease or represents acute infection in an immunocompromised host. To assess the early predictive value for active coccidioidomycosis of the spherulin skin test, coccidioides complement fixation and immunodiffusion antibody studies and coccidioides antigen ELISA in the HIV infected population.

Technical Approach: This is a prospective descriptive study. Subjects will be obtained from individuals participating in the HIV natural history study 86-49 (non-active duty) and HIV infected active duty soldiers who are followed in the WBAMC Infectious Disease Clinic per AR 600-110. Completion date is dependent on number of patients enrolled and severity of their immunologic compromise. Estimated study duration is 5 years.

On entry, a complete geographic history will be obtained to assess travel to Cocci endemic regions (West Texas, Arizona, San Joaquin Valley in California). On entry and every 6 months thereafter, delayed hypersensitivity skin testing will be performed IAW DOD HIV staging. In addition, spherulin 1:100 (Berkeley Biologics) will be included in the battery which is already usual practice in cocci endemic regions. Chest radiograph will be obtained on entry and every 12 months which is current clinical practice during HIV staging. On entry and every 6 months, the following blood tests will be ordered: T cell subset by flow cytometry, quantitative immunoglobulins and SPEP, complement fixation Coccidioides antibodies (sent to Dr. Pappagianis' laboratory at UC, Davis), Coccidioidal precipitins (sent to FSH, TX), serum for coccidioidal antigen (research test) - will be frozen at -70°F initially. On entry and every 6 months, weight will be recorded. On entry and at every subsequent staging, patient will be clinically evaluated by history and physical examination to assess for presence of active coccidioidomycosis.

Progress: Data collection of spherulin skin test, cocci CF and immunodiffusion began in Sep 91. Serial data collection (X1) has been obtained on 27/60 enrollees thus far. Antigen testing of banked serum has not yet begun. No acute infection or reactivation of cocci has been identified in any of the enrollees to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/73

STATUS: Terminated

TITLE: Serum Gastrin and Epidermal Growth Factor Levels in Patients with Adenomatous Polyps and Carcinoma of the Colon

START DATE: Sep 89

ESTIMATED COMPLETION DATE: Unknown

PRINCIPAL INVESTIGATOR: MAJ David M. Maccini

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Edward L. Burkhalter, MC

KEY WORDS: Epidermal growth factor; Colon neoplasm

Study Objective: The purpose of this study is to determine if there is a significant elevation of the serum levels of gastrin and EGF in patients with colon carcinoma and colonic adenomatous polyps when compared to a control population (patients with a normal colonoscopy).

Technical Approach: Measurement of serum gastrin and epidermal growth factor will be performed in three groups of patients. Group one will be patients who are found to have polyps (adenomatous or hyperplastic) at colonoscopy. Group two will consist of patients who are found to have colorectal carcinoma at colonoscopy or surgery. And group three will include patients who have undergone colonoscopy and had a normal examination (no prior history of colonic polyps or cancer). patients will be between the ages of 18 and 99 (male and female) and have no history of other malignancies or peptic ulcer disease. It is expected that most patients will be recruited prior to or after undergoing colonoscopy in the GI Clinic at WBAMC. Indications for colonoscopy will be independent of this study. Twenty patients will be included in each group.

Patients will have ten milliliters of blood drawn at the time their IV is being started for colonoscopy. This will end the patient's participation in the study. Findings at colonoscopy will be noted on the usual endoscopic record used by the clinic (WBAMC form 524). Blood will be take to Clinical Investigation where it will be centrifuged and the serum frozen. Measurement of epidermal growth factor levels will be performed by RIA by an assay previously set up in Clinical Investigations. Gastrin levels will be processed through the Nuclear Medicine Service. Statistical analysis of the data in each group will be performed and compared. A p value <0.05 will be considered statistically significant.

Progress: Project terminated due to PCS of PI.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/36

STATUS: Ongoing

TITLE: Effect of Heart Disease on the Hemodynamic Response to Supine Upper Extremity Exercise (Monitor: COL Davis)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: CPT Timothy W. Martin

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Roger Belbel, MAJ Lawrence Brenner

KEY WORDS: exercise, hemodynamics, cardiac catheterization

Study Objective: Characterize and compare the hemodynamic response to supine upper exercise in patients with and without heart disease.

Technical Approach: Patients who require heart catheterization and do not have exclusion criteria will be identified and counselled by cardiology staff. Consenting patients will be brought to the catheterization laboratory in a fasting, mildly sedated state. From the femoral approach, a Swan Ganz catheter will be advanced to the right heart and a pigtail catheter will be advanced to the left heart. Resting pressure and flow measurements and blood samples will be obtained. The patient will then perform five to eight minutes of supine arm cycle exercise, during which rest measurements will be repeated. Based on the results of rest measurements, angiography, and other clinical information, patients will be categorized as normal or as having coronary artery disease, cardiomyopathy, or valvular heart disease. The response to supine upper extremity exercise will be compared among the groups.

Progress: Forty-five patients have performed supine armcrank exercise during cardiac catheterization. One patient suffered a CVA within several hours of catheterization and his case was reviewed. Reviewer felt complication was not directly related to protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/03

STATUS: Terminated

TITLE: Learning and Behavior Disorders in Children Referred for Allergy Evaluation

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC David L. Michaels

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: A.W. Atkinson, LTC, MC

KEY WORDS: Attention-deficit disorder, Behavior, Allergy

Study Objective: This project will use a questionnaire to assess the frequency and type of learning and/or behavior disorders in children age 5-12 who are referred to the Allergy Clinic for evaluation of presumed allergic respiratory symptoms (rhinitis, asthma).

Technical Approach: Parents of 100 successive children from age 5-12 being referred for allergy evaluation will be asked to complete the Yale Children's Inventory Questionnaire. These will be reviewed and scored by staff of the Developmental Pediatric Service. If significant abnormalities are identified, parents will be contacted and appropriate interventions will be instituted if deemed necessary by the Developmental Pediatrician.

All children with diagnosed allergy will be prescribed customary allergy treatment to include medications, allergen avoidance, and possibly immunotherapy.

One year after the initial evaluation, each child will be recalled for allergy follow-up. The Yale Inventory will be repeated and scores will be compared with those before allergy treatment. Patterns of significant change in specific areas of learning or behavior may indicate beneficial effects from allergy treatment in children with specific problems.

There are no additional risks to subjects who participate in this study. The usual allergy testing and treatment will be carried out as for patients not in the study. The only additional procedure is the completion of the questionnaire.

Progress: Project terminated. PI used some of the data as a pilot abstract, however, discontinued the study when data showed no trend. PI PCS'd.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/22

STATUS: Ongoing

TITLE: Fourth International Study of Infarct Survival (ISIS-4) (Monitor: LTC Lane)

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Gregory Mock

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Carolyn Bernheim, MAJ Roger Belbel

KEY WORDS: Infarct Survival, Captopril, Magnesium, Nitrate

Study Objective: To obtain reliable assessment of the separate and combined effects on vascular mortality of adding three widely practicable treatments to the current standard treatments for a wide range of types of patient (high risk and low risk) with definite or suspected myocardial infarction.

Technical Approach: This will be an international, multi-center, partially double-blinded, partially placebo-controlled, randomized, prospective study. The three study treatments will be randomized in a "2 x 2 x 2 factorial" design. Each patient will be randomized between controlled-release mononitrate vs. placebo, captopril vs. placebo, and magnesium vs. open control. If, as hoped, a total of 40,000 patients is randomized, there will be about 5000 patients in each of the eight possible combinations of trial treatment. The eight possible combinations are: 2) nitrate alone, 2) captopril alone, 3) magnesium alone, 4) nitrate and captopril, 5) nitrate and magnesium, 6) captopril and magnesium, 7) nitrate, captopril, and magnesium, and 8) no trial treatment. Group sizes of 5000 may not be large enough to yield statistically reliable results. But, the factorial design makes the assumption that the effect of the other two trial treatments is equally distributed between the treatment of interest and its control due to the randomization. Therefore, if 40,000 patients are entered, each treatment will have 20,000 patients vs. 20,000 control subjects for data analysis.

Amendment (Jun 92): CPT Mock assumed PI responsibility 1 Jun 92 due to PCS of CPT Chapin (previous PI).

Progress: The first WBAMC patient was enrolled on 16 Aug 91. A total of 30 patients have been enrolled with the following results: 17 patients had confirmed diagnosis of myocardial infarction and 13 patients ruled out for myocardial infarction. Eight patients were sent for CABG or PTCA; all 8 had confirmed diagnosis of MI. Twelve patients were randomized to receive IV magnesium; 18 patients received no IV magnesium. No in-hospital mortality occurred among the enrolled patients and no adverse effects were reported. In the 14 months since the project began, WBAMC ranks #20 in number of patients enrolled of all participating US hospitals.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 76/33

STATUS: Ongoing

TITLE: Diagnostic Adrenal Scanning with ¹³¹I (NP59)

START DATE: Mar 76

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Albert J. Moreno

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: adrenal scanning

Study Objective: To determine the usefulness of ¹³¹I-NP59 in scanning of the adrenal glands. This agent will be used (1) as a screening test for detection of primary aldosterone tumor, Cushing's disease, adrenal cortical adenoma, or pheochromocytoma; (2) to image adrenals in patients who require adrenal venography and are allergic to contrast media; (3) to detect unilateral adrenocortical hypofunction - calcification, metastatic carcinoma, post-venography infarction, etc.; (4) to detect functioning adrenal remnant after adrenalectomy for Cushing's syndrome; (5) to aid in assessment of adrenocortical function in patients who have been on adrenocortical steroid therapy.

Technical Approach: Patients with clinical evidence of adrenal disease will be thoroughly evaluated by an endocrinologist. Following intravenous administration of ¹³¹I-NP59, adrenal scanning will be performed after 7-10 days. The material will be obtained from the Nuclear Pharmacy, University of Michigan. The WBAMC radiopharmacist will perform sterility and pyrogenicity tests on the radiochemical to ensure that radiopharmaceutical standards are met prior to injection.

NOTE: Project was erroneously terminated in Oct 84. Project reactivated in Sep 92 and folder was reconstituted to include required documentation.

Progress: Fourteen patients have been studied since this protocol was approved. The last study performed at WBAMC was in Sep 90 to help determine the cause of aldosteronism as being due to a primary adenoma. No adverse effects noted.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/34

STATUS: Terminated

TITLE: The Effects of Verapamil and Diltiazem on Gastric Emptying

START DATE: Dec 87

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: LTC Albert J. Moreno

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Morakinyo A. Oyewole Toney

KEY WORDS: Gastric Emptying, Calcium channel blockers

Study Objective: Calcium channel blockers are currently indicated in the treatment of several medical problems. Data on the effects of calcium channel blockers on gastric emptying currently is sparse, but potentially important. This study is to determine the effects of verapamil and diltiazem on gastric emptying in normal human volunteers.

Technical Approach: Selection of patients: Twenty healthy (10 male, 10 female) nonpregnant volunteers with an age range of 21-40 will be studied. Patients with any underlying medical problem, on any medication, with a known allergy history to verapamil or diltiazem, or with an abnormal gastric emptying study will be excluded from the study. Patients will also need a normal physical examination, vital signs, EKG, and SMA-20 prior to entering the study. A BHCG will be drawn on all female patients.

Radiation doses: Each patient will have three studies. Each study consists of 1 mCi Tc-99m SCOL and 250 uCi of In-111 DTPA. The target organs for the Tc-99m SCOL and the In-111 DTPA will be the stomach and colon. The stomach may receive approximately 340 m/rad from Tc-99m SCOL. The distal bowel may receive up to 650 m/rads from the In-111 DTPA. These are acceptable levels of radiation exposure.

Patients presenting to the Gastroenterology Service, WBAMC, will be invited to participate in the study. They will be assigned a number for identification purposes. Each subject will undergo study with each drug. A daily history and physical exam will be accomplished.

Gastric emptying: A modification of the technique prepared by Heading et al. will be used. Both solid and liquid phases will be studied. The solid phase will be a standard meal of beef stew impregnated with 1 mCi of 99mTechnetium labeled sulfur colloid. The liquid phase will be 150cc of water combined with 250 uCi of 111Indium labeled diethylene-triamine-pentaacetic acid 111In-DTPA). The time of ingestion of the meal is defined as the midpoint in the period of ingestion. Initial scanning is done every 15 minutes (60 sec images) for a total of three hours. During scanning the patient will be supine, but at all other times they will be seated in a chair.

Methods: Baseline scan: Day 1. If this is abnormal (40% retention at three hours), the patient will be excluded.

Scan 2: Patients on verapamil for three days or diltiazem for one dose. Last dose of the medication will be 30 minutes prior to scanning. The patient will have nothing by mouth after midnight except for medications. The patients will be randomized to receive verapamil or diltiazem first. There will be a one-week minimum of time off the initial medication prior to starting the second medication. A plasma concentration of the drug will be drawn prior to the gastric emptying study.

Scan 3: The patient will receive the second drug in the same format. The patient will be examined daily by an associate investigator during the investigational period.

Statistical analysis: Student t-test

Medications: Verapamil: Dosage schedule will be 80mg by mouth every six hours. The mean elimination half-life in single dose studies ranged from 2.8 to 7.4 hours. After continuous dosing (every six hours for ten doses) the half life increases to 4.5 to 12.0 hours. Therefore, the drug will be administered for three days prior to testing. The last dose will be 30 minutes prior to testing.

Potential side effects: Cardiovascular: Hypotension - 2.9%, peripheral edema - 1.7%, AV block - 0.8%, bradycardia - 1.1%, CHF or pulmonary edema - 0.9%; **Central nervous system:** Dizziness - 3.6%, headache - 1.8%, fatigue - 1.1%; **Gastrointestinal:** Constipation - 6.3%, nausea - 1.6%.

Side-effects with less than 0.5% incidence and where a causal relationship is not certain: confusion, paresthesia, insomnia, somnolence, equilibrium disorders, blurred vision, syncope, muscle cramps, shakiness, claudication, hair loss, macular eruptions and spotty menstruation.

Diltiazem: Dosage schedule will be 60mg by mouth 30 minutes prior to the test. The plasma elimination half life is 3.5 hours whether single or multiple administrations are used; therefore, a single dose is sufficient.

Progress: Project terminated due to lack of volunteers.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/60

STATUS: Completed

TITLE: Emergency Use of VM-26 in Patient with Lymphoblastic Lymphoma, IV_a, High Risk

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: MAJ Michael E Nash

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Lymphoma, Lymphoblastic, VM-26

Study Objective: VM-26 is needed as part of consolidation therapy for 22 y/o male patient with high grade LBL.

Technical Approach: Drug will be obtained from NCI and will be administered in accordance with accompanying instructions.

Progress: Patient received VM-26 per protocol outline with no adverse effects. Project completed.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/57

STATUS: Ongoing

TITLE: NSABP C-05: A Clinical Trial to Assess the Relative Efficacy of 5-FU + Leucovorin with or without Interferon Alfa-2a in Patients with Dukes' B and C Carcinoma of the Colon

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Sep 94

PRINCIPAL INVESTIGATOR: MAJ Michael E. Nash

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Warren Bowland

KEY WORDS: Dukes' B & C carcinoma

Study Objective: This study will evaluate the relative effectiveness of 5-FU plus Leucovorin with and without alfa interferon in prolonging disease free and overall survival in patients who have undergone standard curative resection of Dukes' B and C carcinoma of the colon.

Technical Approach: Details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/74

STATUS: Completed

TITLE: Echocardiographic Standards for Adolescents Based on Tanner Staging

START DATE: Aug 88

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: COL William Pearl

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Martinko, Dr. Stafford, Dept of Pediatrics

KEY WORDS: Echocardiography

Study Objective: To establish echocardiographic standard for healthy adolescents based on Tanner staging, which measures biologic age rather than chronologic age. The new standards will allow a more narrow definition of normal.

Technical Approach: We propose to obtain an echocardiogram on consenting patients presenting to the Pediatric and Adolescent Clinic for school or sport physicals, between 10 and 17 years of age. Tanner staging will be assessed by examiners, which is part of the normal physical examination. Complete physical examinations will be performed and subjects with evidence of chronic illness or heart or lung disease will be excluded. Furthermore, a questionnaire is to be completed by each subject which elicits additional information on athletic activities and health. The patient will be sent to the Cardiology Clinic upon completion of the physical examination for an echocardiogram to be performed by a trained technician.

Echocardiographic data will be measured by computer analysis and reviewed by a pediatric cardiologist. Measurements will include the thickness of the right free ventricular wall, interventricular septum, left ventricular free wall, aortic root, left atrium, aortic valve opening, and each of the identifiable portions of the mitral valve motion. From the data collected, mean values and standard deviations will be determined for males and females in each of the five Tanner stages. Additional data to be collected on each subject will include height, weight, race, and body surface area.

Progress: M-mode echocardiograms were recorded from 298 healthy adolescents between 10 and 16 years of age. Nineteen measured and ten calculated parameters were correlated with subjects' gender and sexual maturity rating. Significant ($p < .05$) differences by gender were demonstrated for 21 of 29 parameters. Sexual maturity rating had a significant effect on 4 of 29 parameters for boys and on 5 of 29 parameters for girls, when controlling for body surface area. Fourteen of 29 parameters in boys and 3 of 29 parameters in girls showed a significant effect of sexual maturity rating when controlling for age. The male adolescent growth spurt in lean body mass is paralleled by a similar growth spurt in left ventricular volume. Published in *Cardiol Young* 1992; 2: 168-174.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/28

STATUS: Completed

TITLE: Retrospective Evaluation of Resting, Peak Exercise and Simulated Altitude Electrocardiograms of Healthy Young Black Males

START DATE: Mar 92

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: COL William Pearl

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: altitude, exercise, hypoxia

Study Objective: To determine if exercise or hypoxia can be used as a noninvasive method of distinguishing between benign and pathological ST and T wave changes.

Technical Approach: Retrospective review of electrocardiograms already obtained on twenty-five Black male basic trainees between 17 and 21 years of age.

Progress: Twenty-five healthy black men between 17 and 21 years of age were evaluated. Their resting and exercise electrocardiograms were recorded at simulated sea level and at a simulated altitude of 4000 m. Sea level exercise caused a reduction in the amplitudes of R waves and a lowering of J points. Exercise at a simulated altitude of 4000 m caused a lowering of the J point in several leads and a reduction of the R wave amplitude in lead aVF. Hypoxia caused a reduction in the amplitudes of the T waves and a lowering of the J points in several leads. These effects of exercise and altitude, to a great extent, eliminated the appearance of "early repolarization", which is very common among young black men. Project completed and published in Journal of Electrocardiology, Vol. 25 No 3, Jul 92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/29

STATUS: Ongoing

TITLE: Retrospective Evaluation of Resting, Peak Exercise and Simulated Altitude Electrocardiograms of Young Black Males with Sickle Cell Trait and Healthy Controls

START DATE: Mar 92

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: COL William Pearl

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Sickle cell trait

Study Objective: To determine if subjects with Sickle cell trait have different electrocardiographic responses to exercise and hypoxia than healthy controls.

Technical Approach: Review of electrocardiograms already obtained on fifty-two Black male basic trainees between 17 and 21 years of age.

Progress: Fifty-four patients have been enrolled. Electrocardiographic measurements have been made for both the controls and the subjects. Data has been entered into a data base and is currently undergoing statistical evaluation.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/64

STATUS: Terminated

TITLE: RV 26, Tri-Service HIV Biopsychosocial Study

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Mar 92

PRINCIPAL INVESTIGATOR: Beverly Simm

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Connie Jensen-Wilczewski

KEY WORDS: HIV

Study Objective:

- a. To consolidate psychosocial data in HIV-infected military medical beneficiaries in a form which lends itself to analysis. This information will be of practical and scientific value for individual participating medical centers, each military service, and the Department of Defense.
- b. To develop analogous databases at tri-service study sites that use identical measures.
- c. To identify and refine useful clinical measures that can be used to predict HIV exposure or transmission risk and risk for psychosocial morbidity.
- d. To develop, pilot and validate a new instrument and methodology that relates HIV and other STD risk behavior data and HIV transmission risk. Such information will be anonymous until and unless sufficient confidentiality guarantees are available to allow for linked data collection.
- e. Develop databases for the following biopsychosocial study areas:
 - psychosocial factors associated with HIV transmission risk behaviors.
 - areas of focus for psychiatric and psychosocial interventions most likely to significantly impact on the spread of infection.
 - evaluation of the role of psychosocial phenomena such as social supports and methods of coping in reducing HIV transmission and HIV-related morbidity in HIV-infected persons.
 - areas of focus for biopsychosocial interventions most likely to prevent neuropsychiatric progress of HIV disease and limit its consequences in seropositives.
 - baseline rates of salient phenomena in seronegatives.
 - evaluation of effectiveness of HIV transmission reduction interventions by using measures from this study as pre-intervention baseline and post-intervention outcome measures.

Technical Approach: All HIV-infected military medical beneficiaries followed by the WBAMC Infectious Disease Service are eligible for inclusion in this protocol. Anticipated enrollment for the 6-month period is 30. The study will be explained verbally and in written form to potential eligible subjects. Consenting subjects will be asked to sign a volunteer consent form. The Anonymous Behavior Survey will be administered by the investigators who are Infectious Disease Service HIV Social Workers. In order to maintain a participant's anonymity, there will be no identifying information collected with the survey. Participants will complete the survey either alone or in a group of no more than 5 people (adequate space will be provided to maintain privacy). The surveys will be collected in a locked box and be sent to the Henry M. Jackson Foundation for data interpretation. Results will be reported only for all information combined across all completed survey, not individuals.

Progress: Study terminated due to inability to enroll a sufficient number of patients (only 10 enrolled) and other job assignments of the investigators.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/49

STATUS: Ongoing

TITLE: The Natural History of HTLV-III Infection and Disease in a US Military Population

START DATE: May 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: PA Gregory E. Martin; MAJ Wellington Sun, MC; Ms. Lynn B. McNicol, RN

KEY WORDS: HIV Natural History

Study Objective: Study the epidemiology of HTLV-III infection in active duty and retired military personnel and their dependents.

Technical Approach: Standard evaluation will be routine medical evaluation, immunological evaluation, laboratory tests, tests for opportunistic infections, HTLV-III viral cultures on body fluids and organs whenever possible. Completion of HTLV-III clinical evaluation form. HTLV-III tests. Counselling, education, and referral of contacts. Follow-up of individuals in the study. Data analysis: disease progression will be studied, as defined by Walter Reed Staging Classification. The effect of variables, including but not limited to age, sex, ethnic background, risk factors, length of infection, and simultaneous viral infections, will be studied.

Addendum: 12 Feb 90 - This protocol was amended to exclude active duty servicemembers. At the directive of the Secretary of the Army, all active duty HIV+ servicemembers are to be clinically staged periodically.

Progress: This ongoing protocol continues to enroll each newly-noted HIV seropositive active duty soldier as part of the US Army's nationwide natural history study of HIV infection. Much of the interval data collection and medical evaluation is mandated by regulation and data is maintained locally in the Infectious Disease and Preventive Medicine Services and in the national USADS data base. Total WBAMC enrollment to date is 171. Many of these individuals are no longer stationed in the Ft. Bliss area, but continue to be followed at their new duty stations, or, if retired, at their local military medical facility.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/22

STATUS: Ongoing

TITLE: Prospective Evaluation of Health Care Workers Exposed to the Blood of Human Immunodeficiency Virus (HIV)

START DATE: Mar 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun, MC; Ms. Lynn McNicol, RN

KEY WORDS: Health care workers, HIV, seroconversion

Study Objective: The objectives of this prospective surveillance project are:

- 1) To estimate the risk of HIV infection in health care workers (HCWs) exposed via the parenteral or mucous membrane route to HIV infected blood, according to type of exposure.
- 2) Describe infection control precautions taken or not-taken to evaluate extent of preventable exposures.
- 3) To describe the clinical natural history and development of laboratory markers of HIV infection in health care workers enrolled in this project who seroconvert to HIV.

Technical Approach: The number of exposed health care workers is expected to be less than 30/year, but is dependent on the number of HIV infected individuals cared for at WBAMC, a population which is increasing in size.

Upon entry into the surveillance project, each exposed HCW will be interviewed and a questionnaire completed collecting the following data: demographic information, use of immunosuppressive drugs, circumstances of the blood exposure, type of infection control precautions used at the time of exposure, any past exposure prophylaxis and information on the source patient. The exposed HCW will be asked to complete a questionnaire concerning risk factors for HIV infection. This confidential report will be completed by the exposed HCW and mailed directly to CDC by the worker. Information collected on this form (CDC 57.42A) will not be released to personnel at WBAMC.

The exposed HCW will be prospectively followed by the investigators for one year with follow up data and specimen collection at 6 weeks, 3 months, 6 months, and one year post exposure. At each follow-up a questionnaire and 10 ml. serum will be sent to CDC. In addition to scheduled follow-ups the exposed HCW must report to the investigator any illness of at least one week duration which occurs in the 12 week period after exposure. If the symptoms are suggestive of an acute retroviral syndrome, the investigator will obtain whole blood for virus isolation + T cell subset (10 ml) and serum (10 ml) for antibody/antigen testing.

Baseline serum samples will be tested for HIV antibody, if negative, HIV antigen will also be evaluated. If a HCW seroconverts a 10 ml heparinized whole blood sample will be requested from the source patient with their informed consent. Viral isolates from the source patient and HCW will be compared using molecular techniques.

Exposed health care workers will be followed for one year post-exposure.

Progress: This protocol is part of the natural history study sponsored by the CDC which tracks all health care workers who are exposed to blood or body fluids of HIV-positive patients during the performance of their jobs. No medical interventions are employed. Study is designed to detect seroconversions only and involves no risk to participating health care workers other than

the necessity of serial blood draws. Eleven health care workers have been enrolled in this protocol. Seven completed the protocol with no evidence of seroconversion during the follow up period. Four health care workers have not yet completed the protocol, but show no evidence of seroconversion to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/66

STATUS: Completed

TITLE: Use of Itraconazole for Treatment of Coccidiomycosis (Monitor: COL Cannady)

START DATE: Jan 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun, MC

KEY WORDS: Itraconazole, Coccidiomycosis

Study Objectives: To assess the efficacy of Itraconazole therapy in fungal disease. The study is a non-blinded, non-crossover study to assess drug efficacy. Medication used will be Itraconazole. Population studies will be those with fungal disease who have failed on standard drug therapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92; no new enrollments. Both patients have no evidence of active infection with stable or slowly falling cocci serum CF Titers. No adverse reactions. FDA drug approval is expected in the near future.

Progress: Study completed. FDA approval of the drug is expected in the near future. The two patients who received itraconazole on this protocol are no longer cared for at WBAMC. Patient who was treated for chronic cavitary pulmonary coccidiomycosis relocated to Colorado Springs area and is currently followed by the Infectious Disease Service at FAMC in Denver. Patient who received itraconazole for over two years for treatment of disseminated coccidiomycosis with left ankle osteomyelitis remains eligible for care at WBAMC but lives in Phoenix, AZ area and recently began CAPD secondary to ESRD (etiology: Amphotericin B nephrotoxicity and uncontrolled hypertension; not a drug side effect). He now has a private infectious disease physician who obtains itraconazole through Janssen. No further enrollments are expected.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/67

STATUS: Ongoing

TITLE: Investigational Prophylactic Use of Zidovudine in Health Care Workers Sustaining a Deep Percutaneous Occupational Exposure to Human Immunodeficiency Virus (Monitor: COL Cannady)

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Lynn B. McNicol, RN; MAJ Wellington Sun, MC

KEY WORDS: Zidovudine, AZT, health care workers, needlesticks

Study Objective: To offer a defined course of zidovudine to HIV negative health care workers within 5 days of a significant exposure to HIV. To assess the safety and tolerance of 200mg zidovudine given orally every 6 hours for 42 days in otherwise healthy persons.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - 3 enrolled; one withdrawn after blood donor found to be HIV-negative. One patient who completed 6-wk course of AZT could not tolerate full dose (200mg QID) secondary to gastrointestinal and neurologic side effects dose. Dose was adjusted to 200mg TID. WBAMC Infectious Disease Service continued to offer prophylactic AZT to health care workers who sustain a significant contaminated needlestick injury. No seroconversions have been documented. Data is pooled with national reporting through CDC in order to hopefully determine AZT's efficacy in this setting.

Progress: Three patients have been enrolled. One patient completed the prescribed 6-week course of therapy with the prescribed dosage regimen; one patient experienced headaches, nausea, and malaise on the full dose regimen but completed a 6-week course of therapy with reduction in dosage; and one patient elected to withdraw due to drug side effects of headaches, nausea, and malaise which prevented her from working. These side effects are all well described with zidovudine therapy and tend to resolve as patients continue to take the drug. None of the three patients suffered any long term effects and all side effects resolved with reduced dosage and discontinued drug therapy. No seroconversions have occurred.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/05

STATUS: Completed

TITLE: A Treatment IND Protocol for the Use of 2'3'-dideoxyinosine (ddI) in Patients with AIDS or ARC Who Are Intolerant to Zidovudine (Monitor: COL Cannady)

START DATE: Dec 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Renata Riley, PA-C; Ms. Lynn B. McNicol, RN

KEY WORDS: Dideoxyinosine

Study Objective: To make ddI available to persons with HIV infection who have developed intolerance to Zidovudine (AZT) and to evaluate the toxicity of ddI in AIDS/ARC patients.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: PI terminated project on semiannual review (Apr 92) due to FDA drug approval. Four patients were enrolled; two withdrew due to pancreatitis problems.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/54

STATUS: Terminated

TITLE: Efficacy of Passive Immunization in the Prevention of Infection Due to Klebsiella pneumoniae and Pseudomonas aeruginosa (Monitor: LTC Lane)

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Naomi Aronson, MC

KEY WORDS: IVIG, passive immunization, Klebsiella pneumoniae, Pseudomonas aeruginosa

Study Objective: (1) To determine the efficacy of intravenous immunoglobulin (IVIG) compared with albumin in reducing the incidence of infection caused by Klebsiella and Pseudomonas bacterial serotypes contained in the two vaccines. (2) To determine whether IVIG delays onset or lessens severity of serotype-specific infection.

Technical Approach: In a double blind, randomized fashion, study participants will receive a one time IV infusion of K-PIVIG (5gms, 7gms, 9gms, or 11gms depending on weight of ≤ 50 Kg, 51-70Kg, or ≥ 91 Kg, respectively) and multivitamins or albumin and multivitamins. All patients will be followed daily for signs of infection while in the hospital for a maximum of 6 weeks. Patients who are discharged prior to this time will be telephoned to ascertain 6-week survival status.

Amendment: Amended infusion time range to 45-90 minutes on the consent form.

Semiannual Review: Apr 92 - 40 patients enrolled. Study placed on hold in Apr 92 due to cluster of 6-7 patients who became hypertensive with study drug/placebo infusion. Product quality control was reviewed.

Progress: Project terminated in Jul 92 with no further enrollments at WBAMC. Of the 40 WBAMC enrollments, 13 died during the course of the study of complications unrelated to study drug or placebo infusion; the high mortality rate is not unexpected given the seriously ill patient population from which study participants were enrolled. Two patients experienced adverse events at the time of study drug/placebo infusion: one experienced bronchospasm and severe systolic hypertension during study drug infusion and the other experienced chest pain after study drug infusion was complete. Both patients had rapid reversal of these complications and both lived the entire six weeks of the study protocol. These adverse events were most likely not related to study drug.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/23E

STATUS: Completed

TITLE: Emergency Use of Itraconazole for Treatment of Sporotrichosis (Patient F.L.)

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Indef

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Sporotrichosis, Itraconazole

Study Objective: Emergency one-time approval sought to treat patient with progressive skin lesions and fever despite amphotericin B who is developing renal insufficiency (creatinine 4.2) in an effort to preserve the patient's life and renal function.

Technical Approach: Itraconazole will be used in accordance with Janssen single patient protocol (JRD 51,211/CC), IND 24,313).

Semiannual Review: Apr 92 - no adverse effects.

Progress: Protocol completed.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/23

STATUS: Completed

TITLE: Use of Itraconazole for Treatment of Sporotrichosis (Monitor: COL Cannady)

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Indef

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun, MC

KEY WORDS: Sporotrichosis, Itraconazole

Study Objective: To assess the efficacy of itraconazole in sporotrichosis in a non-blinded, non-crossover study under the Janssen Pharmaceuticals' protocol (IND 24,313) on patients who have failed available standard therapy (e.g., amphotericin B, ketoconazole) due to lack of efficacy, adverse effects or contraindications for use.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - Patient has no evidence of active infection. In Jan-Feb 92, patient underwent debridement of extensive chronic osteo of the right medial femoral condyle (suspected to be secondary to sporotrix); cultures were sterile. PI will re-evaluate need for further treatment in the next several months.

Progress: Patient treated for over one year and experienced no adverse drug effects and had no evidence of relapse of sporotrichosis. Protocol completed. Itraconazole will be released by the FDA in the new future.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/50

STATUS: Terminated

TITLE: An Open Label Regimen of Videx (2'3'-dideoxyinosine, ddI) in Children with Acquired Immune Deficiency Syndrome (AIDS) Who Have Demonstrated Significant Deterioration or Intolerance to Zidovudine (Retrovir)(Monitor: MAJ Wellington Sun)

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Martin Weiss, MC

KEY WORDS: AIDS, Videx

Study Objective: This open compassionate use protocol is to provide an investigational new antiretroviral agent, 2'3'-dideoxyinosine (ddI), to children with advanced HIV infection who are unable to take zidovudine (Retrovir). Patients will be closely monitored during the course of this protocol to assess drug efficacy and to monitor for signs of drug toxicity or adverse reactions.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Prior to receipt of HSC approval, ddI received FDA approval (Oct 91). HSC returned protocol without action and study was cancelled. No patients were enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/50

STATUS: Ongoing

TITLE: Centocor: HA-1A Efficacy in Septic Shock (CHES Trial-Centocor Protocol #C0041T20, IND #2283)(Monitor: Dr. Hobretsch)

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun; LTC William Lane

KEY WORDS: septic shock, CHES

Study Objective: The primary objective of this trial is to compare the effectiveness of 100 mg of HA-1A and placebo in reducing the 14 day all-cause mortality in patients with septic shock who have documented gram negative bacteremia. The secondary objective of this trial is to assess the safety of HA-1A in patients with septic shock, who have and do not have documented gram negative bacteremia.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Amendment #1 (Sep 92): Changed method of randomization.

Progress: No patients have been enrolled at WBAMC because study drug just recently arrived from manufacturer. This protocol is part of the nationwide Phase III protocol sponsored by Centocor in order to document efficacy of HA-1A monoclonal antibody against the lipid A moiety of endotoxin in the treatment of gram negative septic shock.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/06

STATUS: Completed

TITLE: A Prospective Double-Blind Study of Retrovir in the Treatment of Patients with Early HIV-Associated Immunodeficiency (Monitor: COL Cannady)

START DATE: Dec 88

ESTIMATED COMPLETION DATE: Sep 91

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Shannon M. Harrison (FAMC), MAJ David C. Slagle (WBAMC)

KEY WORDS: Zidovudine in Early HIV

Study Objective:

1. To evaluate the safety and tolerance of chronic administration of RETROVIR (zidovudine) to adult patients with early manifestation of ARC, including those presenting with only HIV-associated lymphadenopathy and a CD4 cell count <500 cells/mm³.
2. To assess the efficacy of RETROVIR therapy in the treatment of HIV disease in these patients. Therapeutic efficacy will be determined by monitoring the following variables.
 - a. Changes in the incidence of progression of HIV disease to more advanced disease stages.
 - b. Changes in clinical manifestation of HIV disease as reflected in objective signs such as weight change, lymphadenopathy, Karnofsky score and performance on tests of neurologic function.
 - c. Prevention of the progressive deterioration of the immune response associated with HIV disease as reflected in changes in CD⁴ cell number and skin test reactivity.
 - d. Changes in levels of HIV viremia/antigenemia in virus-positive patients.

Technical Approach: The ability of RETROVIR to halt or delay early HIV disease progression is the critical clinical objective in the demonstration of therapeutic efficacy. clinical disease will be evaluated as described by the Centers for Disease Control classification system and the Walter Reed Staging System.

For the purpose of this study, the incidence of disease progression will be measured as follows:

1. By the development of severe ARC, characterized by a CD⁴ cell count <200 persisting for a period of at least 3 months and the new development of at least 2 of the symptoms and/or infections listed in appendix VIII. *[Protocol 27,433-15/Project 53 Burroughs Wellcome Co.]
2. By the development of AIDS characterized by the diagnosis of any of the AIDS-defining diseases or disease-related conditions listed in Appendix III.
3. By an increase in Walter Reed classification of one or more stages.

Independent interim and final analyses of disease progression will be done using both systems.

Progress: WBAMC entered 9 patients; two withdrew. Multicenter study completed 30 Sep 91 and evolved into prospective collection and banking of lymphocytes and clinical data on HIV infected individuals taking antiretroviral agents. Central site was FAMC; other sites include DACH, WBAMC, Denver Health & Hospitals, Denver CPCRA.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/40

STATUS: Terminated

TITLE: The Effect of Megestrol Acetate on the Cachexia of Human Immunodeficiency Virus Infection: A Randomized, Placebo-Controlled, Double-Blinded Study. (Monitor: Dr. Lundy)

START DATE: Aug 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Lynn B. McNicol, RN; PA Gregory Martin; 1LT Christine Norris, RD; Ms. Renata Riley, PA-C

KEY WORDS: Megesterol, HIV Wasting Syndrome

Study Objective: Assess the efficacy of megestrol acetate in the treatment of the anorexia and weight loss associated with HIV infection. Conduct a longitudinal analysis of nutritional, biochemical, anthropomorphic and psychosocial parameters in HIV patients receiving megestrol acetate.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: MAJ Sun assumed PI responsibility on 1 Sep due to MAJ Aronson's PCS, but does not wish to continue. Protocol terminated on semiannual review (Apr 92) with no further patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/51

STATUS: Ongoing

TITLE: A Treatment IND Protocol for the Use of Recombinant Human Granulocyte-Macrophage Colony Stimulating Factor (rGM-CSF) in Compassionate Circumstances (Monitor: COL Cannady)

START DATE: Jul 90

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Ruben D. Sierra, MC; MAJ David C. Slagle, MC; MAJ Ricke Weickmum, RPH; Ms. Lynn B. McNicol, RN

KEY WORDS: cytokines, rGM-CSF

Study Objective: To offer Human rGM-CSF to patients with life threatening neutropenia (generally ANC < 500) due to an underlying disease or a therapeutic maneuver, and to assess the safety and tolerance of rGM-CSF in HIV and oncology/hematology patients.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - No new patients enrolled.

Progress: No new patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/05

STATUS: Ongoing

TITLE: Active Immunization of Early HIV Infected Patients with Recombinant gp 160 HIV protein Phase II Study of Toxicity Immunotherapy, in vivo Immunoregulation and Clinical Efficacy (Monitor: COL Cannady)

START DATE: Nov 90

ESTIMATED COMPLETION DATE: Nov 96

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Charles E. Davis (WRAIR), PA Gregory Martin

KEY WORDS: Recombinant gp 160 HIV Protein, immunotherapy

Study Objective: To conduct a Phase II trial of the recombinant HIV envelope glycoprotein gp160 candidate vaccine, in patients with early HIV infection (Walter Reed Stage I-II). Specific objectives include:

- 1) To continue to evaluate the immunogenicity and toxicity of this product;
- 2) To determine the parameters predictive of immunoresponsiveness; and
- 3) To determine the clinical efficacy of immunization with gp160 in the treatment of early HIV infection.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Addendum: Modifies eligibility criteria. Approved by Tri-Service HUC (26 Feb 91), WBAMC HUC/IRB (23 Apr 91) and WRAMC HUC.

Amendments: (1) Deleted recipe skin testing on Day 180 (typographical error); WBAMC IRB notified 16 Jul 91. (2) Day 210 tetanus immunization shifted to Day 240 and Day 210 visit deleted; WBAMC IRB notified 17 Aug 91. (3) Initiated Phase IIB; presented to IRB 21 Apr 92. (3) Booster vaccinations to be given at 2 month intervals; presented to IRB 21 Jul 92.

Semiannual Review: Apr 92. Six patients have completed 240 days with no clinical adverse effects noted. PI expects to enroll approximately 5 patients in Phase IIB.

Progress: Fifteen patients are enrolled and are at various time points of the study. The three most recent enrollments for GP160 Phase IIB took place in September. No adverse effects have been noted. Nationally, the target enrollment of 600 for Phase II has been reached.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/02

STATUS: Completed

TITLE: Experience with the Gianturco-Roehm Bird's Nest Vena Caval Filter

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: CPT Lisa Zacker

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Thomas L. Stoughton, MAJ Roger Belbel, COL William Pearl

KEY WORDS: Gianturco-Roehm Bird's Nest

Study Objective: The aim of this project is to provide one year follow-up on the 11 patients who received BNF placement at WBAMC between 12/89 and 3/91.

Technical Approach: Mechanical interruption of the inferior vena cava (IVC) protects patients with lower extremity deep venous thrombosis (DVT) from pulmonary embolism (PE). It may be life-saving in patients who either cannot be anticoagulated or have had recurrent PE despite anticoagulation. This project reviews the WBAMC Cardiology Department's experience with the Gianturco-Roehm Bird's Nest Vena Caval Filter, (BNF) a device designed for percutaneous implantation and which first became commercially available in 1989. Between December 1989 and March 1991, 11 patients, 7 men and 4 women underwent BNF placement. All had PE and/or DVT and contraindications to or failure of anticoagulation. Included in this study will be a brief review of commercially available vena caval filters, complications of each filter (i.e., migration, IVC thrombosis, recurrent PEs, femoral vein thrombosis) and indications for filter placement. One year follow-up of these 11 patients revealed 5 had dies as a result of underlying malignancies.

Progress: The investigator found the GNF filter to lend itself to easy insertion when pulmonary angiography is performed by femoral approach and proved effective in the management of difficult clinical problems. Project completed and presented at Military College of Physicians Meeting (San Francisco, CA) in Oct 91.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/08

STATUS: Terminated

TITLE: Relationships Among Selected Pre and Post-natal Factors and Perception of Birth

START DATE: Jun 90

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: 1LT Clarke

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Deborah Oakley, Ph.D.

KEY WORDS: Pregnancy, Stress

Study Objective: To examine the birth experiences of civilian women who are married to active duty soldiers. The immediate and short range study aims will be to:

1. Identify perinatal factors which significantly influence and predict women's perceptions of their birthing experiences.
2. Explore relationships between the selected prenatal factors.
3. Communicate results to the military nursing community, military health care providers, and military leaders.

Technical Approach: A non-probability sample of 250 expectant mothers, planning to deliver and receive 6 week postpartum care at WBAMC will be obtained. Subjects will meet the following selection criteria: civilian, married to an active duty Army soldier, able to read and understand English, 32-38 weeks pregnant, experiencing an uncomplicated pregnancy, and anticipating her first delivery.

All prenatal clinic charts at WBAMC will be screened to determine subject eligibility. Data will be obtained prenatally and postnatally using mailed questionnaires and chart audits. An introductory mailing containing a cover letter, a stamped postcard, a stamped envelope, two copies of the informed consent, and questionnaire #1 will be sent to all eligible women. Questionnaire #2 will be sent to each subject approximately six weeks after her delivery as determined by either a returned postcard or a documented delivery. Hospital records of participating mothers and their infants will be reviewed in order to determine the presence of selected complications. Mothers may withdraw from the study at any time by indicating their desire to do so on the postcard provided and returning the postcard to the researcher. No additional data will be requested from subjects who choose to withdraw.

Progress: Project terminated in Mar 92 at the request of Dept of Nursing. All investigators PCS'd.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/64

STATUS: Ongoing

TITLE: The Relationship of Health Beliefs and Self Efficacy to Adherence Levels in Men and Women Who Complete Phase II Cardiac Rehabilitation

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Nov 92

PRINCIPAL INVESTIGATOR: MAJ Susanne Clark

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Mary Kaough RN, MAJ Michael May AN

KEY WORDS: Adnerence levels between genders

Study Objective: To increase compliance levels of positive cardiovascular health habits after completion of Phase II Cardiac Rehabilitation.

Technical Approach: This is a descriptive, correlational study. Ten men and ten women who have completed Phase II Cardiac Rehabilitation will be asked to complete questionnaires concerning health beliefs, self efficacy, and demographic data. Results will be compared to determine whether a significant difference exists between men and women in their health beliefs and self efficacy levels and if there is a relationship to adherence levels to positive cardiovascular health behaviors.

Progress: Subjects have been identified and will be contacted to obtain permission and collect data from the instruments to be administered.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/67

STATUS: Ongoing

TITLE: Wearing of Duty White Uniform by Professional Nurse Managers Invites
Condescension, Encourages Domination, and Affects Power

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: CPT Patricia Gustafson

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: white uniform

Study Objective: This research proposes to investigate how professional nurse managers feel their appearance in the duty white uniforms invites condescension, effects power, and encourages domination in the military health care setting at William Beaumont Army Medical Center. This research will also determine the validity of the tool.

Technical Approach: This will be a pilot study. It will be descriptive/exploratory in nature. Limitations: The lack of a preestablished tool reliability and a small sample return could limit the generalizations drawn from this survey. In addition, because this survey is based on subjects' feelings and perceptions, there are personal variables which cannot be controlled or documented.

Progress: Protocol just approved. Data collection underway.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/68

STATUS: Ongoing

TITLE: Nursing Effects on Mastectomy Patients' Perception of Self Esteem

START DATE: Oct 92

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: LTC Patricia Lutz

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Helene Harris RN, CPT Deborah Bray, MAJ Nancy Bickford

KEY WORDS: mastectomy

Study Objective: The objective of this study is to determine if there is a positive correlation between nursing support and the mastectomy patient's perception of self esteem.

Technical Approach: Patients will be assigned to either Group A (experimental) or Group B (control) dependent upon their ward assignment. Group A (6W nurses) will be given the handouts based on Maslow's Needs (Appendix A-F) which will be discussed during a 15-minute inservice. Group B (6E) nurses will not be inserviced and will not be given the handouts. When the patient is scheduled for surgery, the General Surgery Staff will send the patients to the Acute Surgical Clinic, where they will be asked if they will participate in the study. Patients who agree to participate will be given the Rosenberg Self-Esteem Tool (Appendix I) which will be turned over to the investigators. Surgery is normally scheduled 1-2 weeks later and patients are admitted to either 6E (Group B - control) or 6W (Group A - experimental) with one-to-one nursing care. Three days postoperatively, the same patients will again be asked to complete the Self Esteem Tool and will additionally be asked to complete the Gardner and Wheelers' Nursing Support Scale (Appendix H). The total nursing care given by all staff members will be evaluated. At the end of the proposed two week study, the data will be taken back to the University of Texas at El Paso, where one-way Analysis of Variance will be used to determine if nurses do have an effect on a patient's perception of self-esteem.

Progress: Study to begin in Oct 92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/43

STATUS: Terminated

TITLE: Job Satisfaction in Clinical Head Nurses

START DATE: Jul 90

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC Kathy Mauro

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Jerilyn A. Wadford, AN

KEY WORDS: Headnurse, Nurse, Job satisfaction

Study Objective: To describe the relationship between selected factors and overall job satisfaction in the Army Nurse Corps Clinical Head Nurse.

Technical Approach: A convenience sample of Army Head Nurses at William Beaumont Army Medical Center will be surveyed. The survey will be distributed to all ANC Head Nurses within the facility. An envelope will be provided and participants will be encouraged to complete the survey within 2 days. One week after initial distribution of the survey, each participant will receive a reminder encouraging them to return the survey if they have not already done so or thanking them if they have. Frequency distributions will be computed for all variables. Scores will be summed and divided by the number of items to attain a mean for each subscale. An overall means for the global scale will be attained as a general measure of nursing satisfaction. The data will be further analyzed using the demographics to assess differences in years of active federal service, specialty, sex, months as a head nurse, marital status, dependents, and work hours. Because of the use of a small sample, results may not be generalized to the Army Nurse Corps. The instrument to be utilized is recently developed. Personal variables cannot be controlled or documented because of subjectiveness of the survey.

Progress: Data collection completed, however PI PCS'd prior to analysis of data. Project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL # 91/09

STATUS: Ongoing

TITLE: Assessment of Recalled Medical Reservists' Needs

START DATE: Dec 90

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: MAJ Christine M. Piper

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Recalled medical reservists

Study Objective: To determine the degree of adjustment difficulty that reservists are experiencing and to assess the needs for additional support measures and programs.

Technical Approach: This study will utilize an anonymous voluntary questionnaire. This is a pilot study to survey medical and medical support reservists who were called to active duty to support Operation Desert Shield while assigned or attached to WBAMC.

Progress: Data collection complete and analysis underway.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/37

STATUS: Ongoing

TITLE: Use of Awareness of Stressors to Manage Burnout in Department of Nursing Midlevel Managers

START DATE: May 92

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: MAJ Christine M. Piper

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Stress, burnout management

Study Objective: To identify current levels of burnout in midlevel nursing managers and work-related stressors and increase awareness of stressors in order to address staff burnout more effectively.

Technical Approach: This study will survey midlevel managers in Department of Nursing. Three instruments will be completed prior to an educational offering on burnout and stress management. Subjects will be asked to complete the same three instruments at 1 month, 6 months, and 2 year post workshop to identify any measured changes.

Progress: Data collection began May 92. Two sets of data have been collected with two remaining in Nov 92 and May 93. Due to personnel changes in the Department of Nursing midlevel management positions, the investigator may consider collecting the same data from newly appointed managers which will provide two separate groups of data for analysis and extend the study time six months. Training program for the managers was conducted in May 92 and will be repeated in Nov 92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/66

STATUS: Ongoing

TITLE: Workload Management for Nurses in the Trauma Resuscitation Unit

START DATE: Jan 93

ESTIMATED COMPLETION DATE: Jan 94

PRINCIPAL INVESTIGATOR: MAJ Laura Terriquez-Kasey

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Susanne Clark

KEY WORDS: workload management

Study Objective: To develop an accurate tool to measure nursing workload in the Trauma Resuscitation Unit; to develop an accurate tool to measure trauma patient acuity in terms of nursing care hours; and to develop an accurate tool that can predict nurse staffing needs.

Technical Approach: This is a descriptive, exploratory study of all incoming trauma patients, "code 3" designated for the Trauma Unit beginning 1 October 1992 through 1 October 1993. We will use a specially designed Trauma Resuscitation Acuity Worksheet to calculate nursing care hours for each "code 3" trauma.

Progress: Collection of data began and was stopped in Oct 92 due to data collection problems. Project on hold pending amendment to data collection sheet and method of collection.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/62

STATUS: Terminated

TITLE: The Effects of Psychodrama, Large Groups and Small Groups, on Head Nurses' Burnout, Tedium

START DATE: Jun 89

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: CPT B.J. Thomas

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Conrad Silvani, AN; CPT Danny Davison, AN; Mariva Barajas, DAC

KEY WORDS: Burnout, Anxiety, Work satisfaction

Study Objective: To empirically validate the use of the psychiatric techniques of using psychodrama, small group, and large group interventions by measuring the changes in burnout, anxiety, and work satisfaction.

Technical Approach: The subjects for this study will be the convenience sample of all the head nurses that attend the work shop "Stress and Burnout for Head Nurses".

Three instruments will be used in this study: The Tedium Measure, Spielberger's State-Trait Anxiety Self Evaluation Questionnaire, and Stamps-Piedmonte Index of Work Satisfaction. Data will be collected using all three instruments at the beginning of the work shop after a brief welcome, introduction, and signing of the consent form. Demographic data will also be collected at this time. Only the Tedium Measure and STAI will be self-scored at this time. The results of these scores will be discussed in a large group atmosphere for the rest of the first hour.

The second hour will consist of psychodrama vignettes that all of the participants will have the opportunity to participate in using scripts that have been developed to portray typical difficulties on the nursing units. The scripts have been designed to demonstrate different leadership styles and attitudes that may be encountered on nursing units.

The third hour of the work shop will be small groups that will focus on the feelings and attitudes that the participants had when they were placed in the roles of the vignettes in positions other than the head nurse such as ward clerk, LPN, staff nurse, patient, etc.

The fourth hour will be a large group problem-solving discussion on how to improve attitudes, and decrease burnout and stressors by the inclusion of positive attitudes and conditions in the work place. All three of the instruments will then be re-administered at the end of the fourth hour.

Two weeks after the work shop each of the head nurses will again be administered each of the three instruments by the primary investigator.

The control group, which will consist of the head nurses that do not participate in the workshop, will be contacted on an individual basis and be administered the three instruments after signing a consent form and filling in the demographic data. The second administration of the instruments will take place approximately four hours after the first administration. The third administration of the instruments will take place approximately two weeks after the first two. No intervention will take place between the administration of the instruments. All data sheets will be coded to protect the privacy of the participant. Only the primary investigator will have a master list of participant names and codes that will be secured at all times.

Progress: Data collection was completed and analysis of data was in progress but interrupted by PCS move of PI. Project terminated.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/24

STATUS: Ongoing

TITLE: The Effect of Relaxation Therapy on Patients with Asthma

START DATE: Jan 87

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: Helen Villegas RN

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Asthma relaxation therapy

Study Objective: To measure the effects of relaxation therapy on asthma symptoms, frequency of prn medications, and emergency medical care.

Technical Approach: Fifty intrinsic asthma patients, 20-40 years of age, followed daily in the Allergy clinic, will be involved in participating in this pilot study for 6 weeks. History and biographical data will confirm the diagnosis of intrinsic asthma. Pulmonary function tests (PFT) will be measured on the first visit. PFT will also be recorded on the second and last visit. Patients will keep an asthma diary which will document daily peak expiratory flow rate, asthma symptoms, assessment of mood and use of prn medications and medical care. After 3 weeks, subjects will return to the Allergy Clinic with their completed diaries. Their PFT will be recorded. They will be instructed in the use of a relaxation tape to use each morning upon awakening and each night after retiring. This relaxation tape will include facial muscle exercises and positive thoughts and imaging. Medical news in the Journal of the Medical Association reported in 1983 that the imagination can be used to relieve asthma symptoms while Connors has concluded that tension changes in the facial musculature reliably influences the PEFR. The patient will be given a new asthma diary to record the next 3 weeks. The hypothesis is that the relaxation therapy component of the patient's multifactorial therapy will improve asthma symptoms and decrease medication intake and the need for emergency medical care.

Progress: Twenty-four patients are enrolled. The controls will be enrolled in Nov 92 so that the data will be from the same period. ODS in 1990 and shortage of clinic personnel in 1991 made progress on this part of the research impossible. Investigator will complete on her own time.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/41

STATUS: Ongoing

TITLE: Mixed Venous Oxygenation Saturation in the Critically Ill Patient: Normal fluctuations, the effects of patient care activities, and the effects of circadian influence

START DATE: Jul 92

ESTIMATED COMPLETION DATE: Dec 93

PRINCIPAL INVESTIGATOR: CPT Linda S. Weaver

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: mixed venous oxygenation

Study Objective: The objectives of this study are (1) to determine the normal fluctuations of SvO₂; (2) to determine the effects of routine patient care and other activities on SvO₂ levels; and (3) to determine the effects of circadian influence on fluctuations of SvO₂ and the effects of patient care activities on SvO₂.

Technical Approach: The convenience sample will consist of 50 patients admitted to the MICU who require the placement of a pulmonary artery catheter for medical management. A fiberoptic pulmonary artery catheter capable of continuously monitoring SvO₂ will be placed by the medical resident caring for the patient. Each patient will be observed and SvO₂ will be monitored and recorded on a strip chart recorder during two data collection periods, 0400-0700 hours (Time Group 1 - TG₁) and 1600-1900 hours (Time Group 2 - TG₂). SvO₂ data will be recorded each minute for a 30 minute period of rest. An average SvO₂ (baseline) will be calculated. SvO₂ data for all patient care activities taking place during the remainder of the observation period will be recorded. SvO₂ data within each Time Group will be analyzed using descriptive statistics. SvO₂ fluctuations will be described as percent variation from baseline. Average fluctuation in SvO₂, mean changes in SvO₂ with activity, and mean duration of change in SvO₂ with activity will be calculated for each data collection period and compared using an analysis of variance.

Progress: Investigator failed to respond to requests for annual input.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/24

STATUS: Ongoing

TITLE: Vaginal Hysterectomy; Morbidity with and without Injection of Epinephrine in the Vaginal Cuff

START DATE: May 91

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: MAJ Philip C. Brittain

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew P. Soisson, LTC Carla Hawley-Bowland, LTC Harry C. Crawford

KEY WORDS: Epinephrine, vaginal hysterectomy, cuff injection

Study Objective: To determine if vasoconstrictor use in vaginal hysterectomy increases the incidence of cuff infections and to determine if vasoconstrictor use significantly reduces blood loss during vaginal hysterectomy.

Technical Approach: Patients scheduled for elective vaginal hysterectomy will be prepared for surgery in the usual fashion. The cervicovaginal junction will be injected circumferentially in each patient with 10cc's of one of the solutions described below. All patients will be given similar antibiotic prophylaxis. Estimates of blood loss will be made in conjunction with operating room staff and anesthesia. Postoperative hematocrits will be drawn at similar intervals. Intravenous fluid replacements will be at a 3:1 ratio to estimated blood loss. Specific analysis of what constitutes a postoperative wound infection will be standardized; localized abscess, erythema, marked tenderness, temperature elevation, rising white blood cell count/increasing percentage of immature forms on peripheral smear, tissue necrosis, frank pus, temperature >38 c, negative chest x-ray, and negative cultures of blood and urine. Cuff closures will be standardized among surgeons in the study.

In a double blinded randomized fashion, the pharmacy at William Beaumont Army Medical Center will prepare and code the solution to be injected. The study group will be injected with a dilute solution of epinephrine (1:200,000) in sterile saline, and a control group with sterile saline. Only at the conclusion of the study will the code be broken and data analyzed.

Progress: 62 patients have been enrolled. Recruitment is a little slower than anticipated. No problems with data collection on those enrolled. No adverse reactions have been noted thus far.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/47

STATUS: Ongoing

TITLE: The Clinical Management of Patients with Mild Dysplasia of the Uterine Cervix

START DATE: May 91

ESTIMATED COMPLETION DATE: Aug 93

PRINCIPAL INVESTIGATOR: MAJ Philip C. Brittain

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew P. Soisson, LTC Carla Hawley-Bowland, LTC Harry C. Crawford

KEY WORDS: Dysplasia (mild)

Study Objective: To determine the incidence of HPV infection in young women with histologically proven mild dysplasia (CIN I) of the uterine cervix.

Technical Approach: Patients with dysplastic cervical cells detected by cytology will undergo standard colposcopic examination, colposcopically-directed biopsies of suspicious cervical lesions found during colposcopy, and endocervical curettage. Patients with the following clinical and pathologic characteristics will be considered for study entry: (a) histologically proven mild dysplasia (CIN I) of the ectocervix; (b) adequate colposcopic examination; (c) absence of dysplastic epithelium in the endocervical canal as proven by endocervical curettage. These patients will be thoroughly counseled about study entry. Samples from patients who elect to participate will undergo in-situ DNA hybridization to detect specific subtypes of HPV within cervical cells using the Vira-Type kit. Patients with even last digit SSN will receive standard therapy using cryotherapy or laser vaporization of the transformation zone of the cervix (Group A). Patients with odd last digit SSN will be assigned to the observation group (Group B). All study participants will be monitored every 3 months in the Gynecology Clinic using cervical cytology (PAP Smear), colposcopic examination, and colposcopically directed biopsies of suspicious lesions. All women will be followed for a minimum of 2 years. The sexual consorts of study group patients will be referred to the Male Dysplasia Clinic in the OB-GYN Clinic for Vira Type, colposcopy and colposcopically directed biopsies.

Progress: Thirty-two patients enrolled. Investigator having some trouble recruiting patients due to disclaimer that no pregnancy occur for the two year duration of the study.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/44

STATUS: Completed

TITLE: Effects of Epidural Anesthesia on Trial of Labor after Cesarean Delivery

START DATE: May 92

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: MAJ Philip C. Brittain

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Katherine Foley

KEY WORDS: epidural anesthesia, Cesarean delivery

Study Objective: To determine the incidence of epidural anesthesia at WBAMC; the incidence of trial of labor and success rates with and without epidural anesthesia; and the incidence of operative vaginal deliveries and compare the rates with and without epidural anesthesia.

Technical Approach: This is a retrospective study of all deliveries at WBAMC since 1 January 1988 through 31 December 1991, approximately 6,000 total deliveries. We will review the delivery records for VBAC, trial of labor, and operative vaginal deliveries. We will then calculate success rates and incidences.

Progress: Project complete with 6375 records reviewed. Scheduled for presentation at the Armed Forces District Meeting of the American College of Obstetrics and Gynecology in Norfolk, VA on 2 Nov 92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/40

STATUS: Ongoing

TITLE: Comparison of Azithromycin and Erythromycin in the Treatment of Cervical Chlamydial Infection during Pregnancy

START DATE: May 92

ESTIMATED COMPLETION DATE: May 93

PRINCIPAL INVESTIGATOR: CPT Mark R. Bush

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa

KEY WORDS: chlamydia, azithromycin

Study Objective: To compare azithromycin and erythromycin with respect to efficacy in eradicating cervical chlamydial infection and to compare the incidence and severity of side effects.

Technical Approach: Pregnant patients with positive cervical chlamydial culture will be invited to join the study. Informed consent will be obtained. The patient will be randomized to either treatment arm via a sealed envelope system. The treatment arms are: erythromycin 500mg QID x 7d or azithromycin 1 gram PO x 1. The patient will be given a one page side effect questionnaire at the onset of therapy (see enclosure 4). Both treatment arms will be recultured 14 days after completion of therapy. In the event that a patient cannot tolerate erythromycin 500mg QID dosing secondary to side effects, the regimen will be altered to 250mg QID, as is customary. If she continues to be intolerant she will be considered a treatment failure for erythromycin and offered azithromycin.

Progress: Study progressing according to protocol with 11 enrolled. Target enrollment is 120. No adverse effects noted.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/70

STATUS: Completed

TITLE: Modified Method for Laparoscopic Uterine Suspension

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: CPT Ingrid Chamales

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: uterine suspension

Study Objective: Performing a modification of a medically accepted procedure, with the objective of a smaller incision than the currently used operation. This may shorten total operation time. This is a retrospective study of patients in whom this procedure has been done at William Beaumont Army Medical Center.

Technical Approach: The heretofore described laparoscopic suspensions consist of two low lateral incisions to bring the round ligaments to the fascia in a manner similar to a Gilliam's suspension. Our modification consists of passing a Kelly clamp through the midline suprapubic second puncture, and bringing both round ligaments anteriorly at the midline under direct visualization. The proposed modification would eliminate use the two additional incisions required by previously described laparoscopic procedure.

Progress: Project completed. Data presented at Armed Forces Meeting of American College of OBGYN in Nov 91.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/53

STATUS: Completed

TITLE: Spontaneous Abortion Rate and the Gulf War Mobilization

START DATE: Jul 92

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT James M. Feeley

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa

KEY WORDS: abortion, stress

Study Objective: The purpose of this review is to evaluate in our population the relation between stress secondary to a major troop deployment and SAB, and to evaluate the effect of putative soldiers' exposure to toxic agents on their wives' SAB rate for pregnancies conceived after their return from the Gulf.

Technical Approach: Accumulated service and ward statistics will be reviewed. The number of deliveries will be obtained from the L+D log book, the number of new OB patients and SAB's will be obtained from service statistics reports.

Progress: Project completed and scheduled to be presented at the 31st Annual Meeting of Armed Forces District, American College of OBGYN, in Norfolk, VA (1-5 Nov 92). From the data collected, the investigators concluded that stress or environmental exposure associated with the Gulf War had no affect on the SAB rates in this population.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/27

STATUS: Terminated

TITLE: A Prospective Evaluation of Closure of Subcutaneous Tissue During Closure of Abdominal Incisions

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Jason P. Fontenot

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa

KEY WORDS: Incision, Seroma

Study Objective: To evaluate whether closure of subcutaneous layer at the time of laparotomy closure has any effect on the incidence of hematoma, wound infection, or scar puckering.

Technical Approach: This study will be a prospective, randomized blinded study. Patients will be divided into two groups: (1) subcutaneous tissue will be closed with suture or (2) subcutaneous tissue will not be closed. Only the surgical team will know whether the procedure was performed. Daily evaluation of patient recovery will be performed during hospitalization. The incidence of wound infection, hematoma or abscess formation will be determined at the 6-week postop evaluation. Scar/incision condition and scar development will also be documented at 6 weeks.

Progress: Study terminated; no patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/25

STATUS: Completed

TITLE: The Association Between Race and Risk of Preterm Labor Among Enlisted Women

START DATE: May 91

ESTIMATED COMPLETION DATE: Feb 92

PRINCIPAL INVESTIGATOR: MAJ Frederick Harlass

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CDR Melissa M. Adams (CDC)

KEY WORDS: Preterm labor

Study Objective: We propose a retrospective cohort study of the association between maternal race (black or white) and preterm delivery among the relatively homogeneous population of enlisted Army women who delivered at the four Army medical centers with the greatest number of deliveries. This study presents a unique opportunity to assess the relationship between race and a preterm delivery in a healthy, relatively homogeneous population for whom no financial barriers to prenatal care exist and in which the providers of and content of prenatal care are consistent across racial groups.

Technical Approach: We propose a retrospective cohort study of the association between maternal race (black or white) and preterm delivery among the relatively homogeneous population of enlisted Army women who delivered at the four Army medical centers with the greatest number of deliveries. This epidemiologic study presents a unique opportunity to assess the relationship between race and preterm delivery in a healthy, relatively homogeneous population for whom no financial barriers to prenatal care exist and in which the providers of and content of prenatal care are consistent across racial groups.

We plan to abstract data at four medical centers: Beaumont, Madigan, Walter Reed, and Tripler. Permission to review charts at each of these centers has been granted by the Office of the Surgeon General of the Army. We will abstract data from mothers and infant's charts. The study will include enlisted black or white mothers who delivered a live born infant of any gestational age or a stillborn infant of 20 weeks' gestation or longer from July 1, 1987 through September 31, 1990. We anticipate that most of the mothers will be aged 20-29 years. The infants will be newborns.

Progress: Study completed; results of analysis to be published.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/08

STATUS: Ongoing

TITLE: Obgyn Bowel Training Utilizing the Pig Model

START DATE: Jul 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Carla G. Hawley-Bowland

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Surgical training in residency - GI

Study Objective: This training is designed to teach physicians the basic knowledge and operative skills required to perform basic small and large bowel surgery.

Technical Approach: The laboratory exercise described will concentrate on developing the surgeons confidence in recognizing bowel injuries, resecting and anastomosing small bowel, and large bowel exteriorization. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery consists of small bowel resection and re-anastomosis. The surgical site is then closed and the animal awoken from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted and the training will consist of resecting the colon and creating a colostomy. Afterward, the surgical site will be closed and euthanasia administer while the animal is still anesthetized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Seven pigs have been utilized for training in nine operative episodes (none in FY92). Twelve residents have been trained. Strict adherence to protocol guidelines is maintained.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/33

STATUS: Ongoing

TITLE: OB/GYN Microsurgical Tubal Re-Anastomosis Training Utilizing A Rabbit Model

START DATE: Mar 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Carla G. Hawley-Bowland

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MC

KEY WORDS: Tubal Re-anastomosis

Study Objective: This training is designed to teach resident physicians the basic knowledge and operative skills required to perform microscopic tubal surgery.

Technical Approach: The laboratory exercise described will concentrate on developing the surgeon's confidence in utilizing the operating microscope and microsurgical instruments as well as planning and accomplishing the operative procedures. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery consists of unilateral uterine cornua resection and re-anastomosis. The surgical site is then closed and the animal awoken from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted. The first microsurgical anastomosis site will be re-explored for patency and the training procedure will be repeated on the contralateral cornua. After completion of the procedure euthanasia will be administered as described below.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No rabbits have been utilized this fiscal year.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 86/64

STATUS: Ongoing

TITLE: Genitourinary Tract Surgery Training Utilizing a Pig Model and Comparing Stenting Technique

START DATE: Aug 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Carla G. Hawley-Bowland

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Surgical Training

Study Objective: This training is designed to teach resident physicians the basic knowledge and operative skills required to perform genitourinary surgery while simultaneously evaluating the need for ureteral stenting following the operative procedures.

Technical Approach: The laboratory exercise described will concentrate on developing the surgeons confidence in recognizing GU injuries, resecting and anastomosing ureters, and reimplanting ureters into the urinary bladder. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery will consist of unilateral ureter resection and re-anastomosis. Upon completion of this procedure, the laparotomy incision will be closed and the animal awoken from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted and the training will consist of transecting the contralateral ureter at the point of entry into the urinary bladder and reimplanting the ureter through the bladder wall. Afterward, the laparotomy incision will be closed and euthanasia administered while the animal is still anesthetized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Six pigs have been used in eight operative episodes (none in FY92). Eleven residents were trained in genitourinary surgical techniques. Strict adherence to protocol guidelines is maintained.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/63

STATUS: Ongoing

TITLE: Certification Training: Advanced Laser Laparoscopic GYN Procedures in the Porcine Model

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: LTC Carla Hawley-Bowland

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Laser

Study Objective: To provide training and certification of OB-GYN Surgery Staff in laser and non-laser laparoscopic and vaginal surgical procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The ability to suture during laparoscopy greatly expands the indications for laparoscopic surgery and increases the confidence of the surgeon performing more difficult procedures. There will be two live animal surgical stations and one station where some procedures will be taught with inanimate tissue such as bovine tongue and uterus. After the skin is prepped, an insufflation needle will be inserted near the umbilicus and the abdomen will be filled and maintained with 15mm Hg pressure of CO₂. The insufflation needle will then be removed and replaced with a trocar/cannula for introduction of the video laparoscope which will enable monitoring of the procedure on a video screen. Two to three additional trocars/cannulas will be placed for introduction of laparoscopic graspers, scissors, laser fibers, etc. Training will involve extracorporeal and intracorporeal suturing techniques of various urogenital tissue through the laparoscopic cannulas. The argon-beam and ND:YAG laser will be used to train in techniques of tissue coagulation and excision. Abdominal lymph nodes will also be excised laparoscopically. Training will be conducted on endometrial ablation and tumor excision procedures with lasers and electrosurgery (roller-ball and large loop wire electrodes) via a hysteroscope. If difficulty is encountered with introduction of the scope through the vagina, the uterus will be exposed by laparotomy via a mid anterior suprapubic abdominal incision. Additional training for endometrial ablation and tumor removal will also be conducted with bovine uterus and bovine tongue, respectively.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Three pigs were utilized for training 32 physicians (8 military and 24 civilian) with no intraoperative complications. Training will proceed according to this protocol and the training agreement between WBAMC and Sierra Medical Center.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/48

STATUS: Ongoing

TITLE: Is Measurement of Antibody Excess Cost-Effective After Administration of Rh-Immune Globulin?

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: CPT George M. Kingsley

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Frederick Harlass, MC

KEY WORDS: Rh sensitization, Rh prophylaxis

Study Objective: To perform cost analysis of the post-administration immune globulin excess testing.

Technical Approach: Patients entering the OB system will have ABO/Rh?Prenatal Antibody screen upon entry and at 28 weeks gestation (current standard practice). At delivery, patients identified as Rhogam candidates will be assigned by the attending obstetrician as being Low Risk (no gross placental pathology; no manual placenta extraction; no evidence of placental accreta, increta or percreta, and no evidence of placental abruption or placental previa) or High Risk (one of the above placental factors being present) for fetal-maternal hemorrhage. Patients will continue to receive post-partum Rhogam. Immune globulin excess monitoring will continue. An analysis will be performed to evaluate the cost-effectiveness of the post-administration monitoring for the total population, and comparing the High and Low Risk groups. The following methods of post-administration monitoring will be compared: Leihauer-Betke, Fetal-dex, ELAT (enzyme linked antiglobulin test), flow cytometry, and Rosette test.

Progress: To date, 100 Rh-negative women with Rh-positive infants have been evaluated. Twenty percent of the patients were high risk for fetomaternal hemorrhage by ACOG criteria using Anti-D excell. Four percent of high risk patients and 5% of low risk patients required second doses of RhIG. Enrollment will continue until target is reached and data will be submitted for publication.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/23

STATUS: Ongoing

TITLE: OB-GYN Genitourinary Tract Surgery Incorporating a New Ureteral Anastomotic Device

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: CPT G. Larry Maxwell

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: ureteral anastomosis

Study Objective: The purpose of this study is to compare the efficacy of the UNILINK system, a microvascular anastomotic device, with standard suture techniques in the anastomosis of transected ureters.

Technical Approach: The first surgery will consist of bilateral ureter resection and anastomosis. The UNILINK will be utilized to complete a ureteral anastomosis on the ureter assigned by pseudo random number generation. The contralateral transected ureter will be repaired using suture in a standard repair. Permanent suture will be placed exactly 1 cm. proximally and distally to the anastomotic site to aid in identification at the second surgery. Upon completion of this procedure, the laparotomy incision will be closed and animal awakened from anesthesia. Intravenous pyelograms will be performed immediately following the procedure and repeated at 5 and 15 minutes. Postoperative care will be conducted in a standard fashion. After two weeks, a second laparotomy, and preoperative intravenous pyelogram, will be performed and the anastomotic site will be resected bilaterally at the suture markings. Tissue specimens will be fixed in formalin, imbedded in paraffin, and stored until histologic analysis. Histologic sections every 2 mm. (10 sections/specimen) through the lumens of the anastomotic sites will be performed by Dr. Miles. The cross sectional diameter of each lumen will be measured in serial sections of tissue in order to quantify healing. The anastomotic site repaired with suture will serve as a control against which to compare the UNILINK system.

AMENDMENT (Jul 92): Due to problems with pilot project, methodology was changed to include increased spatulation and the use a J-stent. Ten additional animals were approved for use with the stipulation that only 2-3 animals would initially be entered and results evaluated. The attending veterinarian will decide if the results warrant use of the remaining animals.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Fifteen domestic swine have been used. Results of this pilot study have been compiled and are pending review by the Journal of Surgery in Obstetrics and Gynecology.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/60

STATUS: Completed

TITLE: Adnexal Absorption: A Retrospective Review of Our Experience at William Beaumont Army Medical Center

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT John M. Murphy

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa

KEY WORDS: adnexal absorption

Study Objective: This study reports our experience at William Beaumont Army Medical Center with a relatively rare gynecologic occurrence. We also offer suggestions to facilitate prompt diagnosis of a condition with a truly protean presentation.

Technical Approach: Retrospective analysis of our experience at William Beaumont Army Medical Center.

Progress: Four cases of adnexal absorption syndrome occurred at WBAMC over the past seven years. Three were diagnosed during an infertility evaluation. The incidence in our infertility patient population was 0.5% (3/601). A fourth case was diagnosed at the time of the patient's post-partum tubal ligation. None had a history of previous surgery or symptoms suggestion of adnexal torsion.

Conclusion: Symptoms associated with adnexal torsion may often be absent or minimal, making early and meaningful intervention difficult. Awareness of this phenomenon will facilitate recognition of the condition. Scheduled for presentation.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/45

STATUS: Ongoing

TITLE: Vaginal 5-Fluorouracil Therapy in the Management of Human Papilloma Virus Infections of the Cervix Uteri (Monitor: LTC Rosa)

START DATE: May 92

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: CPT Peter Napolitano

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew Soisson, LTC Carla Hawley-Bowland, Philip Miles, LTC Phillip Day, CPT David Smith

KEY WORDS: Cervix uteri, HPV, 5-fluorouracil

Study Objective: To determine if 5-FU therapy is efficacious in eliminating HPV from the genital tract and to determine if 5-FU therapy will prevent the progression of HPV infections and minor associated cytologic abnormalities (kiliocytotic atypia) to dysplasia.

Technical Approach: Patients will undergo HPV Profile, colposcopic examination, directed biopsies of suspicious lesions, and endocervical curettage (ECC). Patients with a positive HPV Profile will undergo Vira Type to further identify the subtype of the virus. Patients with a normal colposcopic examination or when directed biopsy and ECC excludes a dysplastic process will be counseled appropriately for study entry. Patients who elect to participate will be randomly assigned to one of two treatment regimens: **Group A** will be assigned to the observation only arm and will be followed closely with repeat cytology, HPV Profile, and colposcopic examinations every 3 months for six months. **Group B** will receive 5% topical 5-Fluorouracil cream (1/4 applicator) in the vagina every night for 7 nights. Following therapy, patients will be followed in the same manner as those in Group A.

Progress: Fifteen patients have been enrolled with no documented adverse reactions. Follow up PAPs status post therapy are only now being performed. No early results are available.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/58

STATUS: Ongoing

TITLE: Gonadal Function After Vasectomy

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: LTC Cesar Rosa

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Neal Dunn, MC

KEY WORDS: Vasectomy, gonadal function

Study Objective: To evaluate whether there is any clinical or subclinical evidence of testicular function after vasectomy.

Technical Approach: Approximately 30 active duty males (or others) between the ages 25-40, having vasectomies performed by the Urology Service will be considered suitable candidates. There will be no blinding or randomization necessary. All subjects will receive the same tests. Each patient will serve as his own control. The following tests will be performed:

*Prior to vasectomy -

1

Blood for Testosterone, FSH, LH, PRL, Estradiol. Serum to be frozen for future reference.

2

GnRH test: After the above is collected at - 0 min; similar samples will be obtained at 15, 30, 45, 60, 90 and 120 min after injection of 100 mcg of LHRH (Factrel, Ayerst Labs, New York) at 0 minutes.

3

Serum for antisperm antibodies. To document the incidence of antisperm antibodies following vasectomy. There is evidence of an increased incidence of antisperm antibodies in the circulation after vasectomies.

4

A total of 110ml of blood will be obtained per session (at time of vasectomy, then 6 and 12 months afterwards).

5

Testicular ultrasound to objectively measure size of the testicles.

6

Physical examination (as usual prior to surgery) and testicular size determination with orchidometers (particular attention to testicular tenderness or granuloma formation).

*The same tests will be administered at 6 and 12 months after the vasectomy.

Progress: Fourteen patients had initial GNRH stimulation test and had their vasectomies. Samples were stored in DCI deep freeze. Subjects went to ODS/S. Upon their return as the investigator was getting ready to do the post vasectomy GnRH injection, it was noted that the initial samples had been lost due to freezer malfunction and subsequent thawing of the samples for an undetermined period of time. No adverse reactions observed. Initial group of volunteers

can no longer be used for the study. Investigator plans to begin again.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/17

STATUS: Ongoing

TITLE: A Prospective Study of the Treatment of Functional Ovarian Cyst

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: LTC Cesar Rosa

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MAJ Frederick Harlass

KEY WORDS: *Functional ovarian cyst*

Study Objective: To determine the effectiveness of oral contraceptives in the involution of benign ovarian cysts in a prospective, randomized fashion, comparing it with a population given placebo.

Technical Approach: Patients presenting to the Gynecology Clinic, who on examination are identified as having a suspected functional ovarian cyst, will be invited to join the study. If the patient accedes, randomization into an oral contraceptive versus placebo group will be performed. Prior to the initiation of medication, an endovaginal ultrasound will be performed by the Department of OB-GYN. The result of the endovaginal ultrasound will not affect the treatment of the patient. As a second arm to the study we will derive information which will indicate how effective is the physician's bimanual examination as compared to the endovaginal ultrasound in the identification and follow-up of these functional ovarian cysts. The patient will be followed for 8 weeks or two cycles with an examination both by bimanual examination and endovaginal ultrasound at the end of 4 and 8 weeks of treatment or placebo.

Progress: Nineteen patients have been enrolled with no complications. LTC Rosa assumed PI responsibilities due to CPT Vu's PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/34

STATUS: Ongoing

TITLE: GOG #95/SWO6 #9047, Randomized Clinical Trial for the Treatment of Women with Selected Stage IC & II (A, B, C) and Selected Stage IA & IB Ovarian Cancer. (Monitor: MAJ Michael Nash)

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Oct 95

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: ovarian cancer

Study Objective: To determine if a short course of chemotherapy is more effective than intra-peritoneal radioisotope therapy in the treatment of early stage ovarian cancer and to determine the relative toxicity of each treatment.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - 1 patient enrolled. Patient randomized to P32 treatment arm and received therapy without complication.

Progress: Second patient enrolled. One patient required a 25% dose reduction due to adverse reaction.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/67

STATUS: Ongoing

TITLE: GOG #90, Evaluation of Cisplatin, Etoposide and Bleomycin (BEP) Induction followed by Vincristine, Dactinomycin and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors (Monitor: MAJ Michael Nash)

START DATE: Nov 91

ESTIMATED COMPLETION DATE: Nov 94

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: ovarian germ cell cancer

Study Objective: To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP) followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors. To evaluate the effect of BEP chemotherapy in patients with recurrent or progressive disease during or after previous non-cisplatin containing chemotherapy. To further investigate the relevant prognostic factors. To evaluate the acute and chronic toxicity of such chemotherapy, particularly in gonadal and reproductive function. To evaluate the effect of chemotherapy on menstrual status and reproductive function in patients in whom the uterus and one tube and ovary are preserved.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no patients enrolled.

Progress: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/68

STATUS: Ongoing

TITLE: GOG #93, Evaluation of intraperitoneal chronic phosphate suspension therapy following negative second-look laparotomy for Epithelial Ovarian Carcinoma (Monitor: MAJ Michael Nash)

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Nov 94

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: ovarian epithelial cancer

Study Objective: To evaluate the efficacy of P32 therapy in patients with no residual ovarian cancer and to evaluate the morbidity from intraperitoneal P32 therapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no patients enrolled.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/03

STATUS: Completed

TITLE: GOG # 72, Ovarian Tumors of Low Malignant Potential; A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease (Monitor: MAJ Michael Nash)

START DATE: Nov 91

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: ovarian tumors

Study Objective: To determine the clinical behavior of these tumors; to determine the effectiveness of melphalan therapy on the treatment of these patients; and to determine the effectiveness of Cisplatin on patients who are unresponsive to melphalan therapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: PI terminated protocol on semiannual review (Apr 92). GOG closed the protocol on 1 Mar 92 after targeted patient accrual was obtained. WBAMC enrolled one patient.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/04

STATUS: Ongoing

TITLE: Protocol GOG # 99, A Phase III Randomized Study of Surgery VS. Surgery Plus
Adjunctive radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma (Monitor:
MAJ Michael Nash)

START DATE: Nov 91

ESTIMATED COMPLETION DATE: Dec 96

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: endometrial adenocarcinoma

Study Objective: To determine if patients with intermediate risk endometrial adenocarcinoma, who have no spread of disease to their lymph nodes, benefit from postoperative pelvic radiotherapy. To evaluate how the addition of radiotherapy will alter the site and rate of cancer recurrence in those intermediate risk individuals.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no patients enrolled.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/05

STATUS: Completed

TITLE: GOG #8901, A Phase I Evaluation of Multiple Daily Fraction Radiation and 5-Fluorouracil Plus Cisplatin in Stage II-B, III and IV-A Carcinoma of the Cervix with Negative Para-Aortic Nodes (Monitor: MAJ Michael Nash)

START DATE: Nov 91

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: cervical carcinoma

Study Objective: To determine the toxicity of accelerated hyperfractionated radiation plus 5-Fluorouracil and cisplatin (5-FU, CDDP) in patients with cancer of the cervix. To determine the optimal tolerated dose of hyper-fractionated radiation when combined with 5-FU, CDDP and intracavitary radiation. To assess whether planned treatment breaks will be required in future studies, and to determine the most appropriate length and timing of these breaks.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no patients enrolled.

Progress: Study closed by GOG.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/10

STATUS: Terminated

TITLE: GOG #111, A Phase III Randomized Study of Cyclophosphamide (NSC #26271) and Cisplatin (NSC #119875) versus Taxol (NSC #125973) and Cisplatin (NSC #119875) in Patients with Suboptimal Stage III and IV Epithelial Ovarian Carcinoma (Monitor: COL Raymond Lundy)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: epithelial ovarian carcinoma

Study Objective: To determine response rate, response duration and survival in suboptimal Stage III and Stage IV ovarian cancer treated with two different platinum-based combination chemotherapy regimens. To evaluate the relative activity of a new combination, cisplatin/taxol, as compared to the standard regimen, cisplatin/cyclophosphamide. To further evaluate the toxicities of the new combination of cisplatin/taxol, in this larger patient population.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: PI terminated project on semiannual review (Apr 92). Study terminated by GOG. Future patients will be enrolled under GOG #132.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/13

STATUS: Ongoing

TITLE: GOG # 108, Ifosfamide (NSC # 109724) and the uroprotector Mesna (NSC # 113891) with or without Cisplatin (NSC # 119875) in patients with advanced, persistent, or recurrent Mixed Mesodermal Tumors of the uterus (Monitor: COL Raymond Lundy)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Jan 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: mesodermal tumors, uterus

Study Objective: To confirm reported high response rates of advanced or recurrent mixed mesodermal tumors of the uterus to Ifosfamide/Mesna; to determine whether the addition of Cisplatin to Ifosfamide/Mesna improves response rates or survival in patients with these tumors; and to determine the toxicity of Ifosfamide/Mesna with Cisplatin in patients with these tumors.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no patients enrolled.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/14

STATUS: Ongoing

TITLE: GOG #104, SWOG - 8501. Intraperitoneal Cis-Platinum/Intravenous Cyclophosphamide vs. Intravenous Cisplatinum/Intravenous Cyclophosphamide in Patients with Non-Measurable (Optimal) Disease Stage III Ovarian Cancer (Monitor: COL Raymond Lundy)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: ovarian cancer (optimal)

Study Objective: To carry out a Phase III randomized trial of intermediate dose intraperitoneal cis-platinum (100mg/M²) plus intravenous cyclophosphamide versus intermediate dose intravenous cis-platinum (100 mg/M²) plus intravenous cyclophosphamide for optimal State III ovarian cancer. To evaluate the toxicities and complications of the two combination drug regimens. To determine in the setting of a prospective randomized trial if the human tumor clonogenic assay with a wide range of drug concentration testing can accurately predict pathologic complete response to two-drug combination therapy in the setting of systemic and intraperitoneal drug administration.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - no patients enrolled.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/30

STATUS: Ongoing

TITLE: GOG #122, Whole Abdominal Radiotherapy versus Circadian-Timed Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma (Monitor: COL Lundy)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Apr 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: endometrial carcinoma (advanced)

Study Objective: To compare treatment outcomes (survival and progression free interval) and failure patterns in patients with stages III and IV endometrial carcinoma (< 2cm residual disease) treated with whole abdominal irradiation versus circadian-timed combination doxorubicin-cisplatin chemotherapy. To determine and compare the incidence and type of acute and late adverse events observed with the two treatment regimens.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/31

STATUS: Ongoing

TITLE: GOG #121, A Phase II Trial of High Dose Megestrol (MEGACE) in Advanced or Recurrent Endometrial Carcinoma (Monitor: MAJ Sierra)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Apr 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: endometrial carcinoma

Study Objective: To determine the response rate and progression-free interval in patients receiving high dose megestrol acetate (Megace) for advanced or recurrent endometrial carcinoma. To determine the toxicity of high dose megestrol acetate in such patients. To determine if estrogen/progesterone receptor status is predictive of response.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/32

STATUS: Ongoing

TITLE: GOG #125, Extended Field Radiation Therapy with Concomitant 5-FU Infusion and Cisplatin Chemotherapy in Patients with Cervical Carcinoma Metastatic to Para-Aortic Lymph Nodes (Phase II) (Monitor: COL Lundy)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Apr 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: cervical carcinoma (metastatic)

Study Objective: In this study, patients with cervical cancer who have biopsy confirmed para-aortic lymph node metastases will receive combination chemotherapy consisting of cisplatin and 5-FU intravenous infusion concomitantly with pelvic and para-aortic extended field radiation therapy. The objectives of this study are to assess progression-free survival and overall survival; sites of initial failure; and morbidity of the treatment.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/33

STATUS: Ongoing

TITLE: GOG #107, A Randomized Study of Doxorubicin (NSC #123127) versus Doxorubicin plus Cisplatin (NSC #119875) in Patients with Primary Stage III and IV Recurrent Adenocarcinoma (Monitor: COL Lundy)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Apr 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: adenocarcinoma

Study Objective: The major objective of this study is to determine whether the addition of cisplatin to doxorubicin offers significant improvement in the frequency of objective response, the duration of progressive free interval, and the length of survival as compared to doxorubicin alone.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/34

STATUS: Ongoing

TITLE: GOG #109, A Randomized Comparison of 5-Fu Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy versus Radiation Therapy Alone in Selected Patients with Stages IA2, IB and IIA Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection (Monitor: MAJ Nash)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Apr 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: cervical carcinoma

Study Objective: To determine whether the combination of 5-fluorouracil (%-FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive pelvic lymph nodes, positive parametrial involvement or positive surgical margins following radical hysterectomy and lymph node dissection for stages IA2, IB, and IIA carcinoma of the cervix. To determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/35

STATUS: Ongoing

TITLE: GOG #132, A Phase III Randomized Study of Cisplatin (NSC #119875) versus Taxol (NSC #125973) versus Taxol and Cisplatin in Patients with Suboptimal Stage III and IV Epithelial Ovarian Carcinoma (Monitor: MAJ Nash)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Apr 95

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Carla Hawley-Bowland

KEY WORDS: epithelial ovarian carcinoma

Study Objective: To determine the relative efficacy of regimens consisting of taxol, versus cisplatin and versus a combination of the two drugs in patients with suboptimally debulked epithelial ovarian cancer; to determine which of the three regimens contribute most favorably to progression free interval and survival; and to compare the incidence of audiologic sequela and other toxicities from either of the three regimens.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/51

STATUS: Ongoing

TITLE: GOG #114, Phase III Randomized Study of IV Cisplatin and Cyclophosphamide vs IV Cisplatin and Taxol vs High Dose IV Carboplatin followed by IV Taxol and Intraperitoneal Cisplatin in Patients with Optimal Stage III Epithelial Ovarian Carcinoma (Monitor: MAJ Sheffler)

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Aug 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: epithelial ovarian carcinoma

Study Objective: To compare recurrence-free interval, complete pathologic response, and survival between the standard regimen of intravenous cisplatin/cyclophosphamide and the two experimental regimens: (1) Intravenous cisplatin/taxol and (2) intraperitoneal carboplatin followed by intravenous taxol and intraperitoneal cisplatin in patients with optimal (<1 cm residual) Stage III epithelial ovarian carcinoma. To compare the toxicities and complications of the three treatment regimens. To correlate serial serum CA-125 levels with negative second look and recurrence-free interval.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: One patient enrolled at WBAMC with no chemotherapy complications. Patient continues to do well. Investigator anticipates an enrollment of 1-3 patients per year.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/52

STATUS: Ongoing

TITLE: GOG #135, Evaluation of Drug Sensitivity and Resistance with the ATP-Cell Viability Assay (ATP-CVA)

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Aug 97

PRINCIPAL INVESTIGATOR: MAJ Andrew Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: ATP-CVA

Study Objective: a.To evaluate the correlation between the ATP-cell assay and patient response to chemotherapy in untreated primary epithelial ovarian carcinoma; to correlate laboratory results with the achievement of pathologic CR at time of second look surgery; to correlate laboratory results with progression-free survival; and to correlate single agent and combined agents in vitro studies with clinical outcome. Single drugs as well as drug combinations will be tested in vitro.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/62

STATUS: Ongoing

TITLE: GOG #138, A Phase II Trial of Cisplatin and Cyclophosphamide in the Treatment of Extraovarian Peritoneal Serous Papillary Carcinoma (Monitor: MAJ Sheffler)

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Oct 95

PRINCIPAL INVESTIGATOR: MAJ Andrew P. Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: papillary carcinoma

Study Objective: To determine the response rate, and response duration in patients with extraovarian peritoneal serous papillary carcinoma treated with a combination of cisplatin and cyclophosphamide.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: No patients enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/63

STATUS: Ongoing

TITLE: GOG #134/NCCTG #92-61-51, A Phase III Trial of Taxol at Three Dose Levels and C-CSF at Two Dose Levels in Platinum-Resistant Ovarian Carcinoma

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Sep 97

PRINCIPAL INVESTIGATOR: MAJ Andrew P. Soisson

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: ovarian carcinoma

Study Objective: To determine if the dose of Taxol affects response rate, progression free interval or survival in patients with platinum-resistant ovarian cancer; to compare the toxicities of the three regimens; to compare the efficacy and toxicity of two dose levels of G-CSF (5 micrograms/kg/day versus 10 micrograms/kg/day) in patients who receive the highest Taxol dose (250 mg/m²); and to determine the relationship between peak Taxol plasma concentration and toxicity/response.

Technical Approach: Details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Protocol just approved. No progress to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/71

STATUS: Completed

TITLE: Operative Laparoscopy for Ectopic Pregnancy in a Residency Program

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: CPT Kenneth Vu

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa

KEY WORDS: laparoscopy, ectopic pregnancy

Study Objective: To review our experience with Operative Laparoscopy in the treatment of ectopic pregnancy and to compare operative laparoscopy vs laparotomy.

Technical Approach: Retrospective record review of ectopic pregnancy cases managed at WBAMC by residents under staff supervision.

Progress: Retrospective analysis of 96 surgical data analyses is complete. Preliminary data presented at 1991 meeting of Armed Forces District of American College of OBGYN. Information is being formatted for publication in medical literature.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/30

STATUS: Ongoing

TITLE: Accupressure Bracelets: An Effective Treatment for First Trimester Nausea and Vomiting of Pregnancy

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Feb 93

PRINCIPAL INVESTIGATOR: CPT Gary Wharton

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dan L. Gehlbach, MAJ, MC

KEY WORDS: Accupressure bracelets, Nausea, Vomiting of pregnancy

Study Objective: To investigate whether the use of an acupressure bracelet can effectively treat nausea and vomiting associated with first trimester gestation.

Technical Approach: Pregnant women who complain of significant nausea and/or vomiting for at least one week's duration will be eligible for this study (dependent daughter's under the age of 18 will be excluded from the study as minors). Patients with other identifiable causes of nausea/vomiting, such as viral syndrome, molar pregnancy, thyroid disease, or preexisting gastrointestinal disease, will be excluded. Patients who are unmarried and less than 18 years of age will be excluded, as will those who require hospitalization on their initial presentation to the clinic. Entry to the study will be offered to all eligible patients at their New OB physical, and to patients presenting to the OB Walk-in Clinic who complain of morning sickness. 75 patients will be randomized by card flip into 3 study groups of 25 patients each. Group 1 will consist of dietary instruction alone; Group 2 will receive dietary instruction and the accupressure bracelet; and Group 3 will receive dietary instruction and the placebo bracelet. Specific oral and written instructions will be given by the authors on correct wear of the bracelets: the accupressure bracelet is to be worn snugly against the arm at 3 fingerbreadths above the wrist flexor crease with the bead against the flexor tendons; the placebo bracelet is to be worn at the level of the wrist flexor crease and loosely enough that a finger may be easily slid beneath the band.

On initial presentation and at each of two weekly visits the patient will be weighed on the same scale in the OB-GYN Clinic, and a questionnaire (Figure 1) administered by an independent observer. The authors will review treatment aspects and record routine obstetrical data at each visit. Patients will be given handouts with specific dietary/treatment instructions and will be asked to record prospectively the number of episodes of emesis. Each patient will be followed for 2 weeks.

Additional support will be required by the Brace Shop in preparation of the placebo bracelets.

Progress: Project is ongoing with 43 subjects enrolled to date. Fourteen patients were dropped secondary to failure to follow up as instructed (even after phone contact). No complications have been encountered.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/28

STATUS: Ongoing

TITLE: Evaluation of Phenobarbital in the Prevention of Intraventricular Hemorrhage in the Very Low Birth Weight Infant (<1500gms or 32 Weeks)

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Feb 93

PRINCIPAL INVESTIGATOR: CPT Gary C. Wharton

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Frederick E. Harlass

KEY WORDS: Intraventricular hemorrhage, Phenobarbital

Study Objective: To retrospectively compare WBAMC records where the current standard of care includes phenobarbital administration to any mother suspected or imminently delivering an infant 15gms or less, to those of R. E. Thomason General Hospital (RETGH), where the current standard of care does not include this administration. Through this comparison, an attempt will be made to demonstrate that such administration is beneficial in reducing the incidence and severity of intraventricular hemorrhage in this population as previously suggested.

Technical Approach: This will be a retrospective case controlled analysis of maternal and infant records. WBAMC's experience will be controlled with the experience at RETGH.

Progress: Study ongoing with enrollment of 102 subjects. Six were withdrawn secondary to fetal death, not meeting weight criteria or transfer to another institution.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/70

STATUS: Completed

TITLE: The Male Factor in Cervical Dysplasia

START DATE: Sep 92

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT Gary Wharton

DEPARTMENT: Obgyn

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Peter Napolitano, LTC Carla Hawley-Bowland

KEY WORDS: cervical dysplasia

Study Objective: Analysis of the efficacy of our current evaluation of male consorts of women with cervical neoplasia and analysis of the utility of current diagnostic methods used in this evaluation.

Technical Approach: Retrospective analysis of treatment provided to 115 males (19-55 years old)

Progress: Project completed with enrollment of 115 male patients. Study results suggest that the incidence of penile dysplasia in this population is low and urethral cultures are unnecessary. Scheduled for presentation at the Armed Forces District Meeting, American College of OBGYN in Norfolk, VA (1-5 Nov 92)

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/45

STATUS: Ongoing

TITLE: Comparison of Two Techniques of Estrogen Receptor Assay in Breast Cancer

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Jun 94

PRINCIPAL INVESTIGATOR: CPT Thomas P. Baker

DEPARTMENT: Path

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Tu Huu Nguyen, MC; CPT Gordon Bell, MC; LTC Steven Arny, MC

KEY WORDS: Estrogen receptor assay, breast cancer

Study Objective: To confirm that the immunohistochemical assay is as reliable as the biochemical assay in determining estrogen receptor content in human breast cancer and to determine whether the immunohistochemical assay would be a more efficient method to perform at William Beaumont Army Medical Center than shipping specimens to another laboratory for biochemical assay.

Technical Approach: The study will consist of two phases which can be performed simultaneously.

Phase I: Phase I will be a retrospective evaluation of the estrogen receptor content of the paraffin embedded tissue blocks of the 50 most recently diagnosed breast cancers at WBAMC. The paraffin imbedded tissue will be pre-processed with the Trypsin and Dnase and the immunohistochemical assay will be performed by a single technician. The slides will then be scored in a qualitative and semiquantitative manner as outlined by Cudahy, et.al., and Pertshuk, et.al. Tumors found to contain more than 10% estimated positive cancer cells will be considered estrogen receptor positive. An ocular grid on the microscope will aid in accurately assessing tumor cellularity. The semiquantitative evaluation will be calculated by estimating the intensity of the nuclear staining as 1+, 2+, or 3+ of 200 cells and then multiplying 1, 2, or 3 by the percentage of cells estimated at each intensity. This figure will then be adjusted by multiplication with the previously estimated cellularity values less than 5 will be "zero-trace", 5-18 will be "low-intermediate", and greater than 18 will be "high". The biochemical assay results are expressed in femtomoles (FMOL) of receptor per microgram of DNA. Tumors with values less than 0.10 FMOL will be considered "negative", 0.10-0.30 FMOL will be "low-intermediate", and greater than 0.30 FMOL will be "positive". The results of the two techniques will be compared to determine concordance. All statistical analyses will be performed by means of the chi-squared test.

Phase II: Phase II will be a prospective, blinded evaluation of the estrogen receptor content of breast carcinomas by two methods - the immunohistochemical technique using the Abbot Kit (ERICA) and the biochemical assay done by PathLab. Each breast biopsy specimen is received in the fresh state in the Pathology Department at WBAMC. Standard operating procedure will be followed and a frozen section will be performed if the specimen is grossly suspect for cancer. Once a diagnosis of cancer is made histologically, additional frozen sections will be cut for immunohistochemical processing for evaluation of estrogen receptors. If the specimen contains sufficient tissue for biochemical assay (at least one cubic centimeter of tumor), a specimen will be sent to PathLab for evaluation as per usual procedure. The remaining specimen will be

processed as usual into paraffin embedded blocks for histochemical viewing. Additional sections will again be made for immunohistochemical evaluation also. One histochemical technician will process the special staining as is standard operation in the WBAMC Pathology Department. The slides processed on frozen and paraffin embedded tissue will be read by all pathologists in the department, depending upon the rotational schedule assigned. The evaluators of the slides will be blinded to the results from the PathLab assay. The frozen and paraffin embedded immunohistochemical slides will be evaluated on different days, thus allowing different evaluators to be blinded to the previous result. The results will be reported as previously outlined in phase I. results of the immunohistochemical assays on both fresh frozen and paraffin imbedded tissue will be compared to each other as well as to the results of the biochemical assay to determine concordance. The cost and time involved to obtain a report of the results will also be compared in order to determine the efficiency of the immunohistochemical assay. As stated previously, this study may eventually be expanded through screening of medical records to determine if the immunohistochemical assay is as effective in predicting the response to hormonal therapy as the biochemical assay since this is the ultimate goal of any estrogen receptor assay.

Progress: CPT Baker assumed PI responsibility due to PCS of CPT Price. Estimated completion of Phase I was initially 28 months. Forty-five of the desired 50 cases were completed. However, due to shortage of histotechnology personnel in Department of Pathology, the remaining cases needed cannot be processed. Phase II of the study has not been started due to the same personnel shortage.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/47

STATUS: Ongoing

TITLE: The Effect of Bovine TSH on Hemoglobin Proportions in Adult Rats

START DATE: Jul 92

ESTIMATED COMPLETION DATE: May 93

PRINCIPAL INVESTIGATOR: MAJ Jack T. Pearson

DEPARTMENT: Path

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Thomas Casey; MAJ Walter Critz; Dawn McKell; John Enriquez; Kerry M. Brady

KEY WORDS: hemoglobin

Study Objective: Test bovine TSH's effect on rat hemoglobin chromatogram patterns.

Technical Approach: Phase I: In this phase five adult animals and the litter from one timed pregnancy will be used to gain familiarity with the procedures to be used in this protocol (and described below); cardiac puncture, intraperitoneal injection, performance and preparation of chromatography.

Phase II: This phase will be used to repeat Gilman and Datta's chromatograms. However rather than classic liquid chromatography, this project will utilize HPLC. Twenty adult rats and the litters from 6 timed pregnancies will undergo cardiac puncture. The specimen will be chromatographed. The chromatograms will be compared to establish the previously observed difference in the adult and neonatal pattern and subsequently compared to Gilman and Datta's work.

Phase III: In this phase, 10 adult rats will each be dosed with different concentrations of bovine TSH. After one week, a cardiac puncture will be performed and the specimens tested for T3 RIA and T4 levels. The dose producing a level of hyperthyroidism which is three times normal will be chosen for phase IV.

Phase IV: In this phase, 20 adult animals will have an intraperitoneal injection of bovine TSH. The control group will also consist of 20 adult animals and will receive an injection of sterile normal saline. Each week a cardiac puncture will be performed and the specimen chromatographed.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Six rats have been used. Phase I of the project has taken longer than initially anticipated, however, is near completion. The procedure for chromatography has been completely worked out and preliminary chromatograms on adult and neonatal rats confirm Gilman and Datta's observation of consistent differences in the chromatograms of adult versus neonatal rats. Additionally, all members of the project have become proficient in the animal procedures to be used later in the study. Currently, Phase II is scheduled to begin in November.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/04

STATUS: Ongoing

TITLE: Adolescent Females with Hirsutism and/or Menstrual Abnormalities Suggestive of Polycystic Ovarian Syndrome or Late Onset Congenital Adrenal Hyperplasia

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Jul 94

PRINCIPAL INVESTIGATOR: CPT Suzanne E. Cuda

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Rita L. Svec

KEY WORDS: Hirsutism, Menstrual abnormalities, Polycystic Ovarian Syndrome, Congenital adrenal hyperplasia

Study Objective: To prospectively follow patients with the complaints of hirsutism and/or menstrual abnormalities using standard of care. The data collected from these patients will be collated and compared to previous studies in an attempt to clarify prior research and work out a more streamlines approach.

Technical Approach: Females presenting to the Adolescent Clinic with complaints of hirsutism and/or oligomenorrhea and amenorrhea will be eligible for the study. Patient must be two years past menarche. Patients will sign an informed consent which will allow data collected during their care to be used in a study. Diagnostic work-up and treatment will be according to the accepted standard of care. We propose to combine several approaches to the work-up of these complaints in order to elucidate more information concerning the differences and similarities between patients falling into a particular diagnostic category.

Progress: Twenty patients have been enrolled to date. Investigator needs 45-50 patients to make any conclusions. Enrollment, data collection and treatment per protocol are ongoing.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/35

STATUS: Ongoing

TITLE: A Double-Blind Randomized Trial of Low Dose Captopril in Adolescents with Insulin-Dependent Diabetes Mellitus

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jul 93

PRINCIPAL INVESTIGATOR: CPT Suzanne E. Cuda

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Rita Svec

KEY WORDS: Captopril, Adolescent insulin-dependent DM

Study Objective: To examine adolescent diabetics with persistent microalbuminuria to determine if use of an ACE inhibitor can reduce microalbuminuria.

Technical Approach: On entry into the study, 3 specimens for microalbuminuria and a 24-hour urine specimen for protein and creatinine will be obtained. The mean of the 3 microalbuminuria samples will be used to determine persistent microalbuminuria. If abnormal, the subject will be eligible to participate in the study. Baseline HgA1C, CBC/diff, TFTs, renal functions, and ophthalmology exam will also be documented. Patients will be randomized using a random numbers table into treatment or placebo groups. This will be double-blinded. The treatment group will be started on Captopril at 0.1 mg/kg/dose twice daily. The placebo group will receive similar tablets twice daily. At the end of six months, the groups will cross over and complete the remaining six-month period. Subjects will be followed every 6-8 weeks with measurement of blood pressure, microalbuminuria, HgA1C, renal panel, and 24-hour urines. Compliance with the medication will be followed by counting pills. The treatment period will be 12 months for each subject. Following treatment period, subjected will return in 6-8 weeks for measurement of blood pressure, HgA1C, and microalbuminuria. Results will be analyzed using the paired Student t test.

Progress: One patient enrolled to date. PI still testing to establish eligibility for protocol entry. Thus far, only three patients have met the criteria. PI does not anticipate being able to complete this protocol without involving patients from other medical centers.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/24

STATUS: Ongoing

TITLE: Dietary Treatment of Hypercholesterolemia in Adolescents

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Jul 93

PRINCIPAL INVESTIGATOR: CPT Suzanne Cuda

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Richard Rupp, Martyne M. Beverly

KEY WORDS: hypercholesterolemia (adolescent)

Study Objective: To identify whether adolescents are a group that will need more therapy or a modification of the currently recommended therapy for hypercholesterolemia.

Technical Approach: A flyer will be available at the Adolescent Medicine Clinic front desk which will explain the study to interested adolescents and their parents. If an individual is interested in participating, he/she will be given a laboratory slip for a non-fasting serum cholesterol and triglyceride level and will be asked to provide a phone number.

If the serum cholesterol is greater than 200 mg/dl, the patient will have a fasting lipid profile. Should the level return at greater than 170 mg/dl but less than 200 mg/dl, the individual will be contacted and asked to repeat the test. If the mean of the two tests is greater than 170 mg/dl, the individual will have a fasting lipid profile. Should the individual persistently show cholesterol levels greater than 170 mg/dl or LDL-cholesterol levels greater than 110 mg/dl, he will be asked to make an appointment with either Dr. Cuda or Dr. Rupp, or to set up a time when he can be counselled by Ms. Beverly.

At the appointment the adolescent will fill out a questionnaire covering age, sex, family history of cardiovascular disease, current address and phone number, and prior diet modification for cardiovascular disease. Weight, height, and blood pressure will also be obtained.

The patient will then be randomized into treatment or non-treatment groups. The treatment group will receive counselling on the Step I diet as recommended by the AHA. The treatment group will be followed up in six months and undergo repeat serum lipid and lipoprotein testing.

The non-treatment group will be followed up in six months with repeat blood testing. Should the patient have persistent hypercholesterolemia at follow-up then they will be counselled for the Step I diet and followed clinically.

Progress: After screening 400 patients, 50 patients have been enrolled. During Oct, investigators will be following up on the first patients enrolled to determine if dietary intervention was successful. Patient enrollment will continue through Jan 93.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/43

STATUS: Ongoing

TITLE: Age of Menarche: A Risk Factor for Osteoporosis

START DATE: May 92

ESTIMATED COMPLETION DATE: Apr 93

PRINCIPAL INVESTIGATOR: CPT Suzanne E. Cuda

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Richard Rupp (USAF), COL Ana Rodriguez, COL Gottlieb Turnbull, LTC Albert Moreno

KEY WORDS: osteoporosis

Study Objective: To correlate age at menarche with bone density in adolescent females.

Technical Approach: 200 adolescent females, ages 13-21, who are at least 2 years post menarche will be asked to volunteer for the study. If the eligibility criteria are met, then they will fill out a short questionnaire, complete a dietary survey for calcium intake, and undergo dual-photon absorptiometry of the lumbar spine and proximal femur.

Progress: Thirty have volunteered to participate. Fifteen have had bone densities completed. Nuclear Medicine Service is analyzing the data at present. Investigators hope to attain a total enrollment of 50-75 patients.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/88

STATUS: Ongoing

TITLE: Incidence of *Corynebacterium Haemolyticum* Pharyngitis in an Adolescent Clinic

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Nov 93

PRINCIPAL INVESTIGATOR: CPT Christopher Dillon

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Martin Weisse

KEY WORDS: *Corynebacterium Haemolyticum* Pharyngitis, Adolescents

Study Objective: The incidence and seasonal variation of *corynebacterium haemolyticum* pharyngitis will be determined over a one year period in the Adolescent Clinic at WBAMC.

Technical Approach: All patients (13-20 years of age) presenting to the Adolescent Clinic at WBAMC with a complaint of "sore throat" who receive a throat culture will automatically be included in the study. It will be conducted over a one year period. A checklist of associated signs and symptoms will be used to standardize the information charted on each patient. No additional tests are needed. The throat culturette which would be obtained anyway will be sufficient. In the lab, the culturette will be plated out on the usual blood agar plates, but those from the Adolescent will be marked to be held for 72 hours. Group A beta hemolytic strep can be read at 24 hours (or less), but *corynebacterium haemolyticum* takes 48-72 hours for adequate growth. Those plates with growth suspicious for *Corynebacterium haemolyticum* will be verified using sugar fermentation techniques.

Patients with a positive culture will be contacted and prescribed a ten day course of erythromycin. (The lab will do sensitivity tests periodically on cultures to determine alternate therapies.) The patients will also be requested to return after treatment for a follow-up throat culture to ascertain eradication of infection. Those who have not responded will be tested for co-incident infectious mononucleosis. Household contacts under age 22 will be requested to also have a throat culture (due to the high incidence of positive results in this population shown in Miller's study).

Those patients identified as having *corynebacterium haemolyticum* will benefit by treatment which should decrease duration of illness, recurrence of infection, and propagation to others in the household. Risks are minimal. No invasive tests are being done. Erythromycin (250mg four times a day for ten days) is among the safest of antibiotics. (Its main side effect is nausea, which can be minimized by taking it with food.)

Progress: Study ongoing. CPT Dillon assumed PI responsibilities and MAJ Weisse stepped down to associate investigator. Due to recent advances, an amendment is required and will be forthcoming.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/06

STATUS: Ongoing

TITLE: Perceived Susceptibility to Harm During Adolescence

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: COL John D. Foley

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Lawrence D. Cohn, Ph.D.

KEY WORDS: Risk taking behavior

Study Objective: The aim of the proposed research is to determine if teenagers hold exaggerated beliefs about their ability to avoid injury and illness. Such unrealistic optimism has been found to characterize the judgments of adults, and the proposed research seeks to determine its developmental course during early-, middle-, and late-adolescence. Although established procedures exist for assessing unrealistic optimism, these procedures have not been employed with adolescents. The proposed research will fill this gap. In so doing, the research will test the frequent assertion that teenagers overestimate their own invincibility.

A second objective of the research is to determine if unrealistic optimism contributes to the initiation of adolescent substance use, reckless driving, and other health threatening activities. The association between risk-taking and unrealistic optimism will be examined in adolescents in the general population, as well as adolescents who have been hospitalized due to injuries arising from their own risk behaviors. The goal of this comparison is to determine if teenagers who are unsuccessful at avoiding harm (i.e., hospitalized teens) display the greatest degree of optimistic bias.

A third objective of the research is to determine if unrealistic optimism diminishes when adolescents evaluate dangers for which they are at unique risk. In particular, the study seeks to determine if Hispanic, Black, and White youth show diminished optimism when evaluating the health threats associated with their respective ethnic background (e.g., increased threat of diabetes among Hispanics).

The final objective of the research is to determine if two developmental variables, age and ego development, influence the magnitude of unrealistic optimism displayed by adolescents.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Data collection from 150 adolescent subjects was completed in Sep 92. Health care provider data collection is underway with completion expected in Jan 93.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/08

STATUS: Ongoing

TITLE: Seasonal Occurrence of Adolescent Health Risk Indicators

START DATE: Jan 91

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: COL John D. Foley

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Health risk indicators

Study Objective: To determine if certain indicators of health risk behaviors by adolescents show a seasonal pattern of occurrence.

Technical Approach: Data will be collected retrospectively from outpatient and inpatient clinical records of information previously recorded in the course of providing appropriate medical care for patients. No identification of individuals by name will be necessary. Data from the previous 2-3 years will be utilized as available. Major areas of focus will be sexuality, substance use, and psychologic problems.

Amendment (May 92): Seven revisions have been made to the original study design: (1) Adolescent subjects, ages 15-20, will complete a survey designed to assess their perceived likelihood of encountering 21 illnesses and undesirable life events; (2) Subjects will complete a questionnaire designed to assess if teenagers hold stereotypes of individuals who are victims of illness (e.g., AIDS) and injury (e.g., car accidents); (3) Adolescents (ages 15-20) will be administered a revised version of the Survey of Health Behaviors which includes 9 questions addressing issues of sex and also includes one item assessing steroid use among the respondents' friends; (4) Adolescents (ages 15-20) will complete a questionnaire designed to assess adolescent stereotypes of teen parents. Participants will be shown a 3" by 3" color picture of a teenage girl sitting next to a young child (caption for one-half of the subjects will indicate the child is a baby sister and "sister" will be deleted for the other half). After viewing the photo, all teens will be asked to give their impressions of the target character using a rating scale; (5) Adolescent subjects will complete a task assessing their understanding of uncertainty terms (e.g., probably, possibly, might); (6) Approximately 100 physicians and nurses will complete a task identical to the task described in #5 to determine if physicians, nurses and adolescent patients attribute different meanings to words commonly used to convey the likelihood of health outcomes; (7) Every other subject recruited into the study will be asked to return to the clinic to complete the survey forms a second time. Re-testing will occur between 1-4 weeks after the initial session. The plan remains the same with the exceptions of the following: 100 physicians and nurses will be recruited into the study; adolescents participants will be recruited from Pediatrics and Pediatric Orthopedics; Medical Staff participants will be recruited from Pediatrics and Surgery.

Progress: Previous PI (LTC Imai) desires to keep protocol open anticipating the need to collect more seasonal data. He is in the process of analyzing information collected to date.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/29

STATUS: Completed

TITLE: Ceftriaxone for Outpatient Management of Suspected Occult Bacteremia (Monitor: COL Popejoy)

START DATE: Apr 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Anna I. Heiser

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Suzanne Cuda, MD, Robert Goldbach, MC

KEY WORDS: Ceftriaxone, occult bacteremia, pediatrics

Study Objective: To compare the effectiveness of ceftriaxone versus augmentin in the treatment of children with a possible blood infection.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Semiannual Review: Apr 92 - 95 patients enrolled. No complications noted.

Progress: WBAMC contributed 68 of the 519 patients in this multicenter study. Sixty of the 519 (11.6%) study patients had positive blood cultures; Streptococcus pneumoniae (51), Haemophilus influenzae b (6), Neisseria meningitidis (2) and group B streptococcus (1). Three subgroups of high risk and two subgroups of low risk were identified. The findings show strong association between increasing degrees of leukocytosis with fever and high risk for bacteremia while increasing degrees of fever without leukocytosis was associated with low risk for bacteremia. Children with positive cultures were more often black, had shorter duration of fever and more pronounced leukocytosis pretreatment than those with negative cultures. Those with positive cultures who received ceftriaxone were nearly all afebrile after 24 hours while a significant number who received A/C remained febrile. In the 459 culture-negative children, more A/C-treated children developed diarrhea, had persistent fever, and less improvement in clinical scores after 24 hours than ceftriaxone-treated children.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/61

STATUS: Ongoing

TITLE: Neonate Emergency Procedure Training in the Rabbit and Guinea Pig Model

START DATE: Jul 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Steven W. Jesse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Emergency procedures, Pediatric training

Study Objective: To train physicians who have not been previously trained in emergency management of neonates, but who will be called upon to perform this function in the Neonatal Intensive Care Unit. The rabbit model will simulate the full term human neonate; the guinea pig model will simulate the preterm human neonate.

ADDENDUM #1: Additionally, the rabbit model will be utilized to demonstrate the procedure for instituting and maintaining an infant on an Infrasonic's Infant Star high frequency ventilator.

Technical Approach: This training is designed for junior house staff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands-on attempts by the interns and residents. The housestaff will then rotate through practical skill stations to perform the assigned tasks. The skill stations and animal lab allow the student to observe and practice to proficiency those life-saving skills necessary in the management and stabilization of the neonatal patient. The animal lab will be held on two separate days with a staff neonatologist and staff veterinarian present on both days.

ADDENDUM: If HFV training is to be provided, then following the administration of anesthesia the staff veterinarian or neonatologist will place a carotid artery catheter as follows: A 3 cm ventral longitudinal skin incision will be made in the mid-cervical region. The 2 cm segment of carotid artery will be isolated by sharp and blunt surgical technique. A proximal and a distal 3-0 silk tie will be passed around the carotid artery. After the distal tie is ligated, a 20 ga catheter will be placed into the carotid artery and directed proximally. The proximal tie will then be secured and the catheter will be sutured to the skin. The skin incision will be closed and the patency of the catheter will be maintained with a heparin lock to enable periodic arterial blood collection for blood gas analysis.

High frequency ventilation: While anesthetized, an intubated rabbit will be placed on an Infrasonic's Infant Star HFV, initially on a conventional IMV mode. Monitoring will be done by chest auscultation and arterial blood gas analysis in the Biological Research facility. HFV will be instituted following the Infrasonic's lab outline. The animal will remain in this mode while the ventilation strategy is thoroughly explained and demonstrated to the participating personnel.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, analgesics, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Three rabbits were used in FY92; no guinea pigs were used. Training procedures have strictly followed existing protocol and have been well received by trainees. Competency is judged by staff observation prior to interns beginning clinical rotations. Training is conducted each July for PL-1s and December for remedial training for those who need it as well as interested nursing personnel from NICU.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/65

STATUS: Ongoing

TITLE: Pediatric Intubation Training Utilizing the Feline Model

START DATE: Jul 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Steven W. Jesse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Intubation, pediatric training

Study Objective: This training is designed to teach physicians and other health care professionals basic knowledge and endotracheal intubation skills required to resuscitate a neonate (newborn) or infant.

Technical Approach: The laboratory exercise described below will concentrate on developing the health professional's confidence in establishing an airway. Each new house officer will be required to intubate 2 cats employing a laryngoscope and endotracheal tube.

Animals will be anesthetized with ketamine HCL (22 mg/kg, given intramuscularly), with atropine (0.04 mg/kg, subcutaneously). Up to 2 additional half-doses (11 mg/kg) of ketamine may be given if needed. Pre-anesthesia with tranquilizer (Acepromazine, 0.2 mg/kg, subcutaneously) may be given to allow easier intubation for first-time trainees. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure. Butorphanol tartrate (0.2 mg/kg SC every 8 hours) will be administered after the procedure to alleviate any possible pain.

At the discretion of the instructor, the stages and planes of anesthesia may be defined and assessed by the students. The animal will be placed in dorsal recumbency. Each trainee will visualize the larynx, noting the similarity of the feline larynx to that of the human infant; palpate the larynx externally; and perform visual intubation using the laryngoscope and endotracheal tube.

Two animals will be intubated by each first-time trainee in each laboratory session. Previously trained individuals will use one animal.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Two animals have been utilized. Semiannual use of felines to train pediatric housestaff in emergency life saving (and invasive) procedures has been expanded to include selected obstetrics housestaff and senior NICU nursing personnel. Felines are used solely for intubation training. Training procedures have strictly followed existing protocol and have been well received by trainees. Competency is judged by staff observation. The ferret has been established as the primary model for this type of protocol. Publications from Power et al at

USUHS validate the model. PI to make the decision whether to change models.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/92

STATUS: Ongoing

TITLE: The Effect of Breastfeeding on the Enteral Absorption of Human IgG in the Neonatal Hartley Guinea Pig

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: MAJ Steven W. Jesse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Breastfeeding, Enteral Absorption of Human IgG, Human IgG

Study Objectives: To assess the influence of breastfeeding on the enteral absorption of immunoglobulin in the neonatal guinea pig. And to assess whether such enterally absorbed immunoglobulin retains function in the form of opsonic activity against Type III Group B Streptococcus.

Technical Approach: Multiparous, untimed-pregnant Hartley guinea pigs will be obtained from a commercial source. Dams will be allowed to deliver pups vaginally at term. Pups will be randomly assigned to receive all nutrition via either suckling, (Group A), or via a commercially available animal formula, (Group B). Appropriate nutritional additives (vitamin C, etc.) will be added to the formula by the veterinary staff. Pups in each group will be gavaged shortly after birth with a single dose, 3g/kg(3cc/100g) 10% Human IgG obtained through a commercial pharmaceutical company. This unit dose has been demonstrated in past investigations to result in consistent enteral absorption of enough Human IgG to be easily detected by current methods of analysis.

Serum samples will be collected at 1, 2, 3, 7 and 14 days following the administration of the IgG. Sera will be separated and stored at -4degrees C until analysis.

Positive controls will consist of values from sera obtained from animals from prior investigations who were injected with lg/kg 10% HlgG intraperitoneally. Negative controls will be derived from sera pooled from dams and stillbirths during this current investigation.

Lab analyses:

Serum total Human IgG: Competitive Inhibition

Enzyme Immunoassay (25)

IgG Opsonic Activity: Opsonophagocytic Assay (26)

Volume required:

30 uL sera (60 uL blood) per assay

2 assays/sample = 120 uL (0.12 ml)/sample

5 samples/animal over 14 days = 0.6ml total

Estimated blood volume of newborn guinea pig =

7cc. Blood requirements are thus minimal.

Addendum: 16 Mar 90 - Added Objective: to better define the timing of gut closure for the enteral absorption of human IgG in the neonatal guinea pig.

Method: Newborn Hartley guinea pig pups will be randomized to receive human IgG orally at the following times: birth, 24 hours of age or at 48 hours of age. Pups will also be randomized to be either exclusively breast or formula fed (as per the current protocol).

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: All animal work was completed in 1990. Serum samples are presently being shipped to WRAMC/USUHS for HIgG analysis. Abstract to be written upon completion of blood work for submission to either local or national meeting in Spring 1993.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/91

STATUS: Ongoing

TITLE: Protocol for Determining the Prevalence of Drug Affected Babies in the Military Population

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Scott Knight

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MAJ Steven Jesse, Dr. Gil Handel (TTRAHC-RETGH), CPT John Murphy (Phase I), CPT George Maxwell (Phase II), COL Manuel Schydlower, John Enriquez

KEY WORDS: Newborn, Drug Affected

Study Objective: To determine the prevalence of the use of illicit drugs during pregnancy in a military population.

Technical Approach: This study is to include all pregnant women who present in labor at WBAMC over a 4 month period or 400 patients, and the infants they deliver.

There will be 400 subjects. Two study groups; mothers and infants. A urine drug screen for marijuana, PCP, cocaine and heroin will be done on all subjects. The drug screen is an enzyme immunoassay. This is a test that is not normally done on these type patients. Urine will be collected from all mothers upon admission to labor and delivery, and frozen. All newborn's first void will be collected with a urine bag and frozen. Biweekly both sets of specimens will be sent to toxicology and assigned study identification numbers. The assay will then be performed.

Data will be collected weekly from the toxicology section of the laboratory and analyzed to determine the prevalence of positive drug screens in the mothers and the infants.

Amendment #1 (Sep 90): Added new associate investigators and amended para 7d and 7g.

Amendment #2 (Nov 91): Changed PI to CPT Knight; deleted associate investigators Gordon & Valerie Bell, Howard Oaks & Ingrid Chamales; added LTC Rosa, MAJ Jesse and Dr. Handel as associate investigators. Amendment extended study completion date to Oct 92 and added R.E. Thomason General Hospital (RETGH).

Progress: Study not in full progress due to difficulties in storing and processing samples.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/40

STATUS: Ongoing

TITLE: Measles Immunity in New Housestaff

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Keith P. Ramsey

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Schydlower

KEY WORDS: Measles immunity, medical interns

Study Objective: To determine the prevalence of immunity to measles in a group of health care workers, who are also young adults; to ensure immunity of new housestaff associate investigators; and to be cost-effective in immunizing new housestaff.

Technical Approach: A questionnaire will be administered to newly arriving interns at WBAMC to determine their past history with respect to measles infection. Immunization records will be reviewed to assess the number and timing of immunizations to measles. Sera will be drawn on each new intern for determination of individual immunity using ELISA.

Progress: Data review is currently underway utilizing analyses provided by statistician.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/12

STATUS: Ongoing

TITLE: Incidence of Occult Urethral Human Papilloma Virus (HPV) Infection in Sexually Active Adolescent Males

START DATE: Mar 92

ESTIMATED COMPLETION DATE: Mar 93

PRINCIPAL INVESTIGATOR: CPT Richard Rupp

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Suzanne Cuda, CPT William Nauschuetz

KEY WORDS: HPV (Adolescent)

Study Objective: To find the incidence of HPV infections in sexually active adolescent males and to possibly explore the feasibility of screening males for occult disease.

Technical Approach: The study will include approximately 100 males presenting to the Troop Clinic or the Adolescent Clinic, who are found on routine health screening to be sexually active or with complaints secondary to sexual activity. Sexually active males choosing to participate will be asked to provide a first morning urine. Participating sexually active males presenting with urethritis also will have an additional urethral swab done. These specimens will be tested using HPV DNA detection techniques. Virapap and Viratype kits are sensitive to as little as 10^2 - 10^3 viral particles which can be as few as 100-200 infected cells. The physician will obtain information including patient's age, age at onset of sexual activity, race, prior STDs, number and sex of partners, and whether the patient is circumcised. All patients will have a follow-up appointment to be counselled on positive and negative results. The subjects will be offered testing for other STDs (i.e., HIV, RPR, gonorrhea, chlamydia).

The data should help delineate the epidemiology of occult HPV in sexually active adolescent males. Condylomata are extremely rare in males of this age. With the high rates of infection found in adolescent females it is likely there is a high rate of occult HPV infections in males. From this data, it may be possible to make conclusions about the usefulness of male HPV screening tests. Knowledgeable about his HPV status, a patient will be able to make informed decisions about risky sexual behavior that may protect him and his partners.

Progress: Fifty-seven specimens have been collected. Seven subjects (14 samples) were tested using Virapap and all were negative even though 3 subjects had urethral condyloma. Virapap does not appear to be sensitive enough. We will attempt to check the remaining specimens using 3SR.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/15

STATUS: Ongoing

TITLE: Physiologic Response to Video Games in Adolescents

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Richard Rupp

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Keith Ramsey

KEY WORDS: video games

Study Objective: To show if there are possibly adverse physiologic cardiovascular changes while playing the video game Tetris and to see if these changes are more pronounced in novices vs. veterans of the game.

Technical Approach: Adolescent patients will play video games while their blood pressure and pulse are monitored in the clinic. No concerns for safety in the study due to the low incidence of seizures and the low risk of tendinitis since subjects will not be playing for extended time periods. Two subjects will participate in each session. Subjects will take turns playing Tetris for 10-minute periods.

Progress: Fifteen subjects participated. Statistical analysis is all that remains.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/20

STATUS: Completed

TITLE: Demographics of Military Dependent Children and Adolescents: Projections for the Military Pediatric Health Care System

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Richard Rupp

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Manuel Schydlower

KEY WORDS: health care, adolescents, military dependents

Study Objective: The planned 25% reduction in the active duty force by 1996 aims to create a smaller but effective military. This will still require provision of high quality health care for eligible dependents. Presently, there are 2.27 million military dependent children (age 0-19 years old) who are in the pediatric patient population. This study will look at the demographics of this population and how the downsizing of the military would effect its characteristics and health care needs.

Technical Approach: Demographic, retrospective data available from the Defense Enrollment Eligibility Reporting System (DEERS), DD Form 1172 and Real-Time Automated Personnel Identification System (RAPIDS) will be retrieved to identify the sex, age, dependency status and branch of service of military dependents 0-19 years old.

Progress: The United States government provides health care for one of the largest beneficiary populations in the world. Of the 2.27 million children who are dependents of uniformed services personnel, approximately 796,500 (35%) are adolescents 13-19 years old. While the majority of dependent children 0-19 years of age are dependents of active duty personnel (74.7%), close to half of the adolescents (47.7%) are dependents of retired personnel. As a result of recent geopolitical world changes and a perceived decreased threat to national security, the military has planned a 25% reduction of the active duty force by 1996. This will tend to reduce the younger dependent pediatric population and raise the mean age of beneficiaries in the 0-19 years age range who are eligible for health care. Pediatricians in the military and civilian contract physicians need to prepare for increased health care of older pediatric patients, particularly adolescents.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/21

STATUS: Completed

TITLE: Telephone Management of Acute Pelvic Pain in Adolescent Females by Adolescent Clinics

START DATE: Feb 92

ESTIMATED COMPLETION DATE: May 92

PRINCIPAL INVESTIGATOR: CPT Richard Rupp

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Keith Ramsey, COL John D. Foley

KEY WORDS: telephone management, adolescent clinic

Study Objective: This study will evaluate the appropriateness of the telephone advice given to an adolescent female with a mock scenario of an ectopic pregnancy.

Technical Approach: An adolescent female will be trained and rehearsed for a mock scenario involving the symptoms of an ectopic pregnancy which is a potentially life threatening event. She will phone adolescent clinics asking for advice. She will also be trained to complete the Advice Evaluation form. Prior to terminating the call, she will inform the called individual that she is a "mock patient in a mock scenario".

Progress: Telephone management of thirty-five clinics was evaluated according to the final disposition. Appropriate management included arranging to see the patient that day or referring the patient to another facility (i.e., emergency department) to be seen that day. Sixty-three percent of the clinics gave appropriate advice; 37% gave inappropriate advice. Non-professional personnel rendered the advice in over 60% of the calls. This study indicates a need to reevaluate the telephone management of adolescents to ensure appropriate advice is provided by the proper personnel.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/55

STATUS: Ongoing

TITLE: Parents Opinions about Disorders of Vigilance in their Children with Attention Deficit Disorder

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Aug 93

PRINCIPAL INVESTIGATOR: LTC Robert Sayers

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Alva W. Atkinson

KEY WORDS: Primary Disorder of Vigilance (PDV)

Study Objective: Through the use of a parent questionnaire, determine the incidence of symptoms of Primary Disorder of Vigilance (PDV) in a population previously diagnosed with Attention Deficit Disorder (ADD) or being evaluated for ADD. Furthermore, this project will seek to differentiate this symptom cluster (PDV) as either a unique diagnosis or a subtype of ADD.

Technical Approach: The Developmental Pediatric Clinic at WBAMC follows approximately 180 patients with the diagnosis of ADD. Patients who are taking medication for ADD are seen in clinic at least every three months and parents come in for a brief interview on progress and refill every month. During one of these routine follow-ups, the parent will be asked to complete a questionnaire which addresses the major criteria for PDV for both the child and his/her parents. These criteria are taken directly from the article "Primary disorder of vigilance: A novel restlessness, and sleepiness" by Weinberg describing this "new" disorder.

Progress: LTC Robert Sayers assumed PI duties due to Dr. Richardson's PCS. Data collection continues. Data from 109 questionnaires were subjected to descriptive and factor (Varimax rotation) analyses. For the children, two factors were isolated. One represented the construct of "arousal" reflecting behaviors such as arousal, tiredness, and lethargy. The other represented the construct of "inattention" reflecting behaviors such as decreased attention, daydreaming, restlessness, and disorganization. Similar factors were found in analyses of biological mothers and fathers. The question about kind temperament did not factor in either group nor as a separate construct. There was a significant correlation for the two factors with each other only for the mothers ($p = <.01$). A significant correlation ($P = <.01$) was also found between the child and father "inattention" factors but not between child and mother factors. Only 4% of children exhibited marked symptoms for "arousal" factor questions and only 3% exhibited similar responses for both factors (needed to diagnose PDV). Thus, in our population, the incidence of PDV appears to be much lower than that initially suggested.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/01

STATUS: Ongoing

TITLE: Retrospective Analysis of the Association between Attention Deficit Disorder and Central Auditory Processing Problems

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Jun93

PRINCIPAL INVESTIGATOR: MAJ Lilliam Sierra

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC AW Atkinson, LTC Richard Dennis, Mary C. Knott

KEY WORDS: ADD, CAPP

Study Objective: Two hypotheses will be addressed: (1) Central auditory processing problems (CAPP) occur in high frequency (>20%) among patients diagnosed with Attention Deficit Disorder (ADD) and (2) the incidence of CAPP in ADD will be represented equally among the subtypes of ADD (ADD with hyperactivity and ADD without hyperactivity).

Technical Approach: The medical records of patients assessed by Developmental Pediatrics Clinic for ADD and by Audiology and Speech/Language Clinics during 1989-1990 will be reviewed. Data will be collected for age, grade, diagnoses, auditory and language evaluation results. Specifically, data from the audiologic assessment data from the SCAN (central auditory processing battery) will be collected. From the language evaluation, the overall receptive and expressive language assessments (normal, mild moderate, or severe) and the TOKEN test results will be noted. Data will be studies for frequencies and association using descriptive and simple comparative statistics. The investigators consider this a pilot study which will potentially be the basis of a prospective, more tightly controlled large study.

Progress: 72 subjects have been entered. Investigators are still collecting data and adding new patients to the protocol and hope to publish the results.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/59

STATUS: Terminated

TITLE: Emergency Use of Recombinate in Patient with Hemophilia A, Factor VIII Deficiency

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: Dr. Jerry J. Swaney

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Hemophilia

Study Objective: To use recombinant DNA Factor VIII (Recombinate) to avoid exposure to any contaminants since this is a pure synthetic product.

Technical Approach: Patient is a 5 month old male newly diagnosed with Hemophilia A, Factor VIII deficiency who has not required any replacement factor infusion to control bleeding. The emergency IND was requested to have Recombinate available until a formal IND is procured. Drug will be obtained from Baster Healthcare Corporation (Hyland Division) through the Regional Hemophilia Center, Univ of Texas Health Science Center at Houston. Recombinate will be administered in accordance with drug company protocol.

Progress: Protocol terminated; parents elected to do otherwise.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/58

STATUS: Ongoing

TITLE: Emergency Use of Erwinia Asparaginase for Treatment of Acute Lymphocytic Leukemia (Patient R.G. 3076)

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: Dr. Jerry Swaney

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: lymphocytic leukemia

Study Objective: To increase the response rate of acute lymphoblastic leukemia (ALL).

Technical Approach: Patient developed an allergic reaction to asparaginase produced by *Escherichia coli*. Erwinia asparaginase is to be substituted for the E. coli-based produce for the remainder of the protocol (18 of 20 doses).

Progress: Patient receiving L-Asp (Erwinia) intramuscularly weekly without problems.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/59

STATUS: Ongoing

TITLE: Emergency Use of Erwinia Asparaginase for Treatment of Acute Lymphocytic Leukemia (Patient C.H. 3759)

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: Dr. Jerry Swaney

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: lymphocytic leukemia

Study Objective: To increase the response rate of acture lymphoblastic leukemia (LLL).

Technical Approach: Patient developed an allergic reaction to asparaginase produced by Escherischia coli. Erwinia asparaginase is to be substituted for the E. coli-based produce for the remainder of the protocol (18 of 20 doses).

Progress: Patient receiving L-Asp (Erwinia) per protocol without problems.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/62

STATUS: Ongoing

TITLE: Medical Experience of The Third Armored Cavalry Regiment During Operations Desert Shield and Desert Storm

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: MAJ Glenn M. Wasserman

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Brian Martin MC (FAMC); CPT Howard Oaks MC; MAJ Harold McAdoo DC; CW2 Richard Harvey (3ACR PA); CDR Bruce Merrill (NAMRU III); CDR Craig Hyams (NMRI)

KEY WORDS: Gulf Crisis, Persian Gulf Crisis, military medicine

Study Objective: The aim of this project is to review and analyze the military, medical experience of first and second echelon medical units attached to a forward line unit (The Third Armored Cavalry Regiment) during Operations Desert Shield and Desert Storm.

Technical Approach: Data will be obtained primarily from retrospective review of preventive medicine disease surveillance data, self-completed questionnaires (Fourth Squadron), stool culture and ova & parasite analysis, and after action reports. There will also be anecdotal reports and data from the medical troop commander, dentist, acting psychiatrist and a physician assistant.

Progress: Original paper is now three papers covering (1) Operation Desert Shield, (2) Operation Desert Storm, and (3) Preventive Medicine. This was necessary because of the volume of data and information. Co-authors for each paper will be adjusted according to the amount of input or contribution to that paper.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/25

STATUS: Ongoing

TITLE: Prevalence of Hypogammaglobulinemia in Children with Recurrent/Persistent Otitis Media

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Jul 93

PRINCIPAL INVESTIGATOR: MAJ Martin E. Weisse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: hypogammaglobulinemia, Igb deficiency

Study Objective: To determine the prevalence and extent of IgG deficiency in otitis prone children.

Technical Approach: Patients meeting the criteria below will have the study explained to them, and after informed consent is obtained, blood will be drawn for 1) complete blood count with differential, 2) quantitative immunoglobulin A, E, G, M, and 3) immunoglobulin G subclasses. If patient has an acute infection with fever at the time of clinic visit, the tests will be drawn at the next visit that the patient is seen and the acute infection is resolved.

Children 1 to 10 years of age presenting to pediatric clinic with history of 3 episodes of acute otitis media in the preceding 6 months, or duration of serous effusion ≥ 3 months after an episode of acute otitis media, will comprise the study population.

All patients will be followed by the principal investigator and the lab results explained. Treatment options/considerations based on clinical and laboratory evaluations will be discussed and most appropriate and acceptable therapy will be implemented.

Progress: Present enrollment (29 patients) is going slightly slower than anticipated. but investigator anticipates reaching an enrollment of 100 by Jul 93.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/39

STATUS: Ongoing

TITLE: A Randomized, Placebo Controlled Study of Immunoglobulin Therapy for Patients with Symptomatic Hypogammaglobulinemia (Monitor: MAJ Wasserman)

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Jul 93

PRINCIPAL INVESTIGATOR: MAJ Martin E. Weisse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Bruce Veit, MAJ Larry Tremper, MAJ Dennis Beaudoin

KEY WORDS: Immunoglobulin

Study Objective: To determine if oral gammaglobulin effects clinical improvement and increased immunoglobulin levels in patients with symptomatic hypogammaglobulinemia.

Technical Approach: Patients who meet study criteria and are enrolled into the study will be randomly assigned to one of two groups. One group of patients will receive a gammaglobulin preparation by mouth, at a dose of 50 mg/kg per dose twice weekly for three months, then will be crossed-over to receive a placebo (orange juice) on the same dosage schedule for an additional three months. The second group will receive the placebo for the first three months, and be crossed over to receive the gammaglobulin preparation for the second three months. We intend for the study to be a randomized, double blind, placebo controlled trial. The dose of gammaglobulin we will use is equivalent to 400 mg/kg per month (the usual dose of intravenous gammaglobulin is 300-400 mg/kg every 3-4 weeks). Serum IgG peak and trough levels will be monitored monthly for the six month study period.

Progress: Present enrollment (5 patients) has been less than expected with several parents declining to participate. In addition, the patients have been relatively infection-free throughout the study period which will/may make our results less meaningful.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/58

STATUS: Completed

TITLE: Designing and Conducting a Full-Day PROFIS Training Session for Personnel at Army Medical Centers

START DATE: Aug 92t

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: CPT Kim C. Strunz

DEPARTMENT: Psnl

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Susan A. MacManus (USF)

KEY WORDS: PROFIS training

Study Objective: The objectives of the study are to: (1) examine the viability of a one-day PROFIS training exercise format for PROFIS personnel assigned to an Army medical center (WBAMC); (2) present the findings to the Commander, WBAMC, the Commander, 131st Field Hospital at Ft. Bliss, and Commander, Health Services Command; and (3) submit the research findings for consideration for publication in a professional journal (e.g., The Journal of the US Army Medical Department).

Technical Approach: The study will be based on survey data generated from PROFIS participants' post-training day evaluations (questionnaire attached). The survey was distributed to all 96 participants; usable responses were received from 87 (a 91% completion rate). Simple descriptive statistics will be utilized to analyze the data. Results will be reported for all participants and then broken out by officer rank (field grade, company grade). Responses to the question asking the degree to which participants personally benefited from the PROFIS training day will also be broken down by branch/category (Medical Corps; Nurse Corps; Medical Service Corps; Enlisted) and by deployment status during Desert Storm operations (deployed; not deployed).

Progress: Project completed and article submitted to Journal of the US Army Medical Department in Aug 92 (acceptance still pending). Only 87 of the 96 questionnaires were usable. A comprehensive one-day training exercise can be an effective PROFIS training approach at Army medical centers, as shown by this post-training analysis of such an exercise at WBAMC. Over two-thirds of the nearly 100 participants said they found the unique one-day (twelve 30-minute classes) PROFIS training somewhat or very beneficial from a personal perspective. The article describes the organizational format and nature of the training and presents participants' ratings of each class and their recommendations for improvement. It also contrasts the views of field and company grade officers.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/23

STATUS: Completed

TITLE: Evaluation of HBV Immunization Using a Series of Two Heptavax and One Recombivax

START DATE: Mar 90

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: Karlyn Pearl

DEPARTMENT: PrvMed

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Ana Ortiz, MC; COL William Pearl, MC

KEY WORDS: HBV Immunization

Study Objective: To evaluate if completing the immunization process of active duty personnel with Recombivax after they have received their first two doses with Heptavax will increase their hepatitis surface antibody titers to levels similar to those receiving the conventional three doses of Heptavax. In addition, will like to find out if their titers are similar a year later.

Technical Approach:

Group A - Control: Fifty patients who have received two doses of Heptavax and are ready to receive the third dose (6 months since their first vaccine, and 5 months post the second vaccine) will be studies. Blood for hepatitis surface antibodies will be obtained at the time of their third immunization, three weeks later, and a year later.

Group B - Study Group: Fifty patients who had received the second dose of Heptavax and are ready to receive their third dose (Recombivax) will be studied. Blood for Hepatitis-S antibodies will be obtained at the time the third vaccine is due, three weeks later, and a year later. These patients will be receiving Recombivax.

Patients will be selected to participate in the study group as follows. As patients present to receive either the Heptavax or the Recombivax, every other one will be asked to participate in the study.

Progress: One hundred patients were enrolled. The increase in titer three weeks after the third immunization was significantly less in those who received a third dose of recombinant vaccine than in those who received a third dose of serum vaccine. One year after receiving the third immunization, those who received the combined regimen had a lower hepatitis B surface antigen titer than at the time of the third immunization. Those who received three doses of serum derived vaccine did not demonstrate this decrease in titer. Investigators conclude that a regimen combining serum and recombinant hepatitis B vaccines may not be as protective as the standard immunization schedule. Those who began immunization with serum vaccine and concluded with recombinant vaccine should be monitored for an accelerated fall in serum antibodies.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/10

STATUS: Ongoing

TITLE: Assessment of Risk Factors for HIV Infections Among Active Duty U.S. Army Personnel with Documented Recent HIV-Antibody Seroconversion

START DATE: Feb 91

ESTIMATED COMPLETION DATE: Dec 96

PRINCIPAL INVESTIGATOR: Karlyn K. Pearl

DEPARTMENT: PrvMed

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Arthur R. Morton; Henry Rodriguez

KEY WORDS: HIV seroconversion

Study Objective: To assess demographic and behavioral determinants associated with new HIV infections. Incident cases are the only population which allow us to investigate important features of the current HIV infection epidemic. Risk factors and their relative significance as determinants of HIV infection will be assessed by comparing medical, demographic, and behavioral histories of active duty personnel recently infected with HIV with histories of individuals who have not seroconverted over a similar time period.

Technical Approach: The study will be conducted using a case-control design. A case will be defined on the basis of HIV-Ab seroconversion (positive Western blot in duplicate). Controls will be randomly selected HIV-Ab negative active duty personnel at the same posts where cases occur, and will be matched to each case on: Age (+/- 2 yrs), race/ethnicity, grade category (junior enlisted, senior enlisted, officer), and length of service in the Army. Two controls will be recruited for each case. Controls must have been tested negative for HIV-AB no earlier than three months before the positive test date of their matched case. Based upon standard methods for determining required sample sizes in a case-control study and the expected number of HIV-AB seroconverters, a 2-year study period is anticipated. All active duty personnel with confirmed HIV-Ab seroconversion will be eligible for inclusion in this study. Cases will be identified each month by review of the USAHDS data base. Physicians in charge of the HIV testing and evaluation programs at posts from which cases are reported will be contacted by WRAIR and asked to invite incident cases to participate in this study. This study is designed to ensure strict confidentiality. All links between name, social security number, or other identification and study numbers are destroyed after the interviews are completed at the study site.

Progress: Sixteen subjects have been enrolled at WBAMC. Study has been extended to include Phase II which will cover Jan 93-Dec 96. Results of Phase I are expected to be available in Spring 1993.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 87/71

STATUS: Ongoing

TITLE: Emergency Procedures Laboratory (Carpine Model)

START DATE: Jul 87

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Michael Peterson

DEPARTMENT: PCCM

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Emergency procedures laboratory

Study Objective: To train accredited physicians who are not dealing with emergencies on a day-to-day basis, but may be called upon to perform this function. The goat model will simulate the human emergency patient.

Technical Approach: Cricothyroidotomy, venous cutdown, chest trauma management, and peritoneal lavage procedures will be accomplished in accordance with training manuals for each procedure.

Progress: Investigator failed to respond to requests for annual input. No training sessions were conducted in the past year.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/19

STATUS: Ongoing

TITLE: Emergency Life Support Training for Paramedics in the Small Ruminant (Ovine or Caprine) Animal Model

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Michael Peterson

DEPARTMENT: PCCM

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Ronald Liss

KEY WORDS: Emergency Life Support Training

Study Objective: This training will enhance the paramedics' capabilities of administering emergency lifesaving procedures to patients with emergency medical conditions which require establishment of airways, venous access, and chest trauma management.

Technical Approach: The emergency life support training program is designed for paramedics who are primarily responsible for providing first echelon care to the critically injured patient. Procedures taught will be according to the American College of Surgeons (ACS) Committee's Advanced Trauma Life Support Course. Initial assessment and management of specific types of injuries are presented to the student through lecture and slide presentations. Students then rotate through animal laboratories associated with the lecture content previously presented. The animal laboratory allows the student to observe and practice to proficiency those life-saving skills necessary in the initial management and stabilization of the trauma patient. The animal laboratory is approximately 2-3 hours per cycle. Each animal station will consist of one instructor and four to five students.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: PI PCS'd. Associate investigator failed to respond to requests for annual input.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/42

STATUS: Completed

TITLE: Improving Patient/Health Care Provider Interaction within an Army Medical Center

START DATE: Jun 92

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Mark A. Davis

DEPARTMENT: Psy

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Dwayne Marrott

KEY WORDS: Patient/provider interaction

Study Objective: To design an intervention that will require little additional staff/physician time, yet is effective in enhancing patient-physician communication and satisfaction through increasing patient involvement in care; and to assess the efficacy of this intervention on increasing patient satisfaction; increasing patient perception of involvement and sense of control over the medical treatment rendered; increasing patient information seeking; and increasing patient decision making without significantly increasing physician time expenditure.

Technical Approach: This is a posttest-only control group design, double-blind study. Independent variable: Intervention letter encouraging greater participation in treatment through questioning and decision making. Dependent variables include Patients' satisfaction as measured by the Medical Interview Satisfaction Scale; Patients' perceived involvement in treatment as measured by the Perceived Involvement in Care Scale; Patients' level of information seeking as measured by the information-seeking scale of the Autonomy Preference Index; Patients' level of decision making as measured by the decision making scale of the Autonomy Preference Index; Experimental Group receives packet with intervention prior to medical interview and questionnaire following interview; Nonspecific Treatment Control Group receives packet with educational information prior to medical interview and questionnaire following interview; Physicians receive "physician questionnaire" on each patient; and Subject selection involves random assignment to treatment versus control group.

Progress: Project completed in Jun 92. Study examined a brief intervention to improve patient-provider interaction within an internal medicine clinic setting. The intervention group showed greater overall and effective satisfaction with the medical interview. No differences were observed between groups on patients' perceived involvement in care or preference for decision-making or information-seeking. Results submitted to Journal Psych.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/39

STATUS: Ongoing

TITLE: Metamemory Functioning in Alcoholics

START DATE: Nov 91

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: COL Al K. Morris

DEPARTMENT: RTF

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Philip H. Marshall, Jack D. Gold

KEY WORDS: metamemory functioning

Study Objective: Metamemory refers to one's ability to make predictions about one's memory functioning. Alcoholics often report difficulties with memory. This study will determine to what extent these difficulties are related to metamemory.

Technical Approach: Subjects will first sign the informed consent form. They will then take the short intelligence test and fill out the biographical survey. They will then complete the FACT RETRIEVAL test.

Progress: Investigator failed to respond to requests for annual input.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/59

STATUS: Terminated

TITLE: Animal Model (Ovine) Laboratory, Advanced Trauma Life Support Course (ATLS)

START DATE: Jun 1988

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Warren F. Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Steve Carey, MC

KEY WORDS: Trauma

Study Objective: To train accredited physicians who are not dealing with major trauma on a day-to-day basis, but may be called upon to perform this function. The goat model will simulate human trauma.

Technical Approach: Animal Procedures

1. Cricothyroidotomy
2. Venous Cutdown
3. Chest Trauma Management
 - a. Needle decompression
 - b. Tube thoracostomy
 - c. Pericardiocentesis
4. Peritoneal Lavage

Training manuals will be used for each training procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Protocol terminated and replaced by WBAMC #92/18.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/42

STATUS: Ongoing

TITLE: Fiberoptic Endoscope Cholecystectomy in the Porcine Model

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

MAJ Stephen Carey, MC; CPT Anthony J. Canfield, MC; CPT Dennis Eastman, MC; CPT Steve Bodney, MC.

KEY WORDS: Fiberoptic Endoscope Cholecystectomy

Study Objective: To determine feasibility of conducting cholecystectomies at WBAMC with endoscopic equipment rather than a laparoscope. The experience gained by the professional staff will enable them to develop proficiently to perform such operations in human patients and to determine if additional equipment will be required for the conduct of this procedure.

Technical Approach: No surgical procedures will be conducted without the administration of general anesthesia. Anesthesia will be administered and monitored by Dr. O'Hair and animal care specialists in the Biological Research Service. The animals' food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. After the skin is prepped, an insufflation needle will be inserted and the abdomen will be filled with CO₂. A trocar will be placed near the umbilicus for introduction of the fiberoptic video endoscope to enable monitoring of the procedure on a video screen. Two to three additional trocars will be placed for introduction of alligator forceps. The cystic duct and artery will be bluntly dissected free, double ligated or clipped, and transected. The gall bladder will be dissected free from the liver bed by sharp, blunt, and electrosurgical techniques. The laser may be used to control hemorrhage and to cut adventitial tissue. Once free from hepatic parenchyma, the gall bladder will be approximated to the body wall and drained with suction. After the bladder is decompressed, it will be pulled through one of the central trocar puncture sites.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: This pilot training protocol was terminated because WBAMC #91/13 has been approved to replace it.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/13

STATUS: Ongoing

TITLE: Resident Training in Laparoscopic and Open Stapling Techniques

START DATE: Mar 91

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Laparoscopic training

Study Objective: The objectives are to teach the surgical staff and residents proper thoracic and abdominal laparoscopic procedures utilizing stapling instruments and suturing techniques and proper open stapling techniques utilizing the multitude of gastrointestinal staplers, including the TA, GIA, EEA instrumentation, the LDS instrument and the Liga Clip Appliers.

Technical Approach: Both video laparoscope and open surgical training techniques will be conducted in the porcine model. The experimental design is such that one or both of the techniques will be conducted on each animal. When both laparoscopic and open techniques are utilized, the laparoscopic techniques will precede the open procedures. The determination of the techniques to be conducted will be done at the time of the training session and will be dependent upon the knowledge and expertise of the residents and staff being trained. After anesthesia induction, the following procedures will be conducted:

(1) Video laparoscopic - Abdominal: cholecystectomy, gastrectomy, small bowel resection, nephrectomy, hysterectomy, splenectomy and partial hepatectomy. Thoracic: esophagectomy, pulmonary resections and vagotomies will be performed utilizing the various stapling instruments and liga clips.

(2) Laparotomy (Open) - Abdominal: A midline incision from the xiphoid process to the pubis will be made. Then a multitude of gastrointestinal staplers, including the TA, GIA, EEA instrumentation, the LDS instrument and the Liga Clip Appliers will be utilized to complete end-to-end, side-to-side colon and small intestinal anastomosis. Additionally, anastomosis will be completed between portions of the small intestine; from the small intestine to stomach and colon; and between the colon and rectum. Transection of the stomach, colon and small intestine will also be performed. Pulmonary: Transection of pulmonary tissue, bronchi, pulmonary arteries and veins will be performed utilizing the various instruments through an intercostal incision.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: COL Bowland assumed PI responsibilities due to LTC Runke's PCS. Thirteen porcine models were utilized for training during FY92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/37

STATUS: Ongoing

TITLE: Certification Training: Lasers in Urology in the Porcine Model

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Fernando L. Diaz-Ball

KEY WORDS: Laser training, Urology

Study Objective: To provide training and certification of Urological Surgeons in laser cystoscopic procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The animals' food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. Surgical Procedure: A cystoscope will be introduced through the urethra into the urinary bladder. Methylene blue 2% in N saline will be infused in to various regions of the urinary bladder mucosa for training with the ND:YAG laser and other lasers, such as the CO₂, Argon, or KTP. Laser surgery training will include techniques from the external urethral os to the urinary bladder and possibly the ureters. If difficulty is encountered with introduction of the cystoscopy via the urethra (since the urethral os is up to 4 cms inside the vagina, anteriorly) the urinary bladder will be exposed by laparotomy via a mid anterior suprapubic abdominal incision. Urethral laser procedures can then be conducted by retrograding the cystoscope through the bladder neck. If larger vesicular tumors are required for laser excision or vaporization training, segments of the rectus muscle will transplanted into the bladder mucosa acutely. The bladder will then be closed with 3-0dexon. Training is scheduled for a maximum of six (6) WBAMC surgeons and ten (10) Sierra surgeons.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No training was conducted.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/38

STATUS: Completed

TITLE: Certification Training: Lasers in Pulmonary and Otolaryngology in the Ovine Model

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: COL Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Miller F. Rhodes

KEY WORDS: Laser training, Pulmonary; Laser training, Otolaryngology

Study Objective: To provide training and certification of pulmonary/ENT surgeons in laser laryngoscopy, bronchoscopy, and esophagoscopy procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The animals' food will be withheld for a period of 24 hours prior to surgery. Wool will be sheared from the neck and cranial thorax. The sheep will be placed in dorsal recumbency. Surgical Procedure: Simulated tumor implantation- A 5 cm vertical incision will be made at the level of the cricothyroid membrane. A small segment of sternothyroid muscle will be resected and transplanted through the cricothyroid membrane to simulate a laryngeal tumor. Sternothyroid muscle will also be resected and transplanted into the esophageal lumen via a 1 cm incision in the esophageal wall to simulate esophageal tumors. The tracheal and esophageal incisions will be closed with 3-0 dextron. Procedures will be repeated as necessary to simulate additional tumors for excision training. Tumor excision- An endoscope will be inserted through the mouth into the airway or the esophagus depending on the training procedure. A laser fiber will be inserted through the endoscope channel and use in training in tumor excision or vaporization with the ND:YAG laser and other lasers, such as the CO₂ or KTP, if available. Training is scheduled for a maximum of six (6) WBAMC surgeons and ten (10) Sierra surgeons.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Project completed; no animals used in FY 92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/12

STATUS: Ongoing

TITLE: Combat Trauma Surgery Using a Portable contact Nd-(YAG) Laser

START DATE: Feb 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John McPhail, MC; CPT Michael J. Snyder, MC; MAJ Steven Carey, MC

KEY WORDS: Laser training, Surgery

Study Objective: The main purpose of this laboratory will be to train physicians who are involved in the care of trauma victims, in the use of the Neodymium (Nd):YAG laser in surgery, and to familiarize them with the laser's applications in trauma management.

Technical Approach: Prior to the actual experiments, each participant in the protocol will be instructed in the safety precautions and the proper use of the (Nd)-YAG laser. Two animals will be used to demonstrate proper technique to the surgeons participating. After proper instruction, two surgeons and one to two assistants will perform the procedures on each animal, allowing each surgeon to be the primary surgeon on two operations. The actual operations will proceed as follows: Each animal will undergo one survival and one non-survival abdominal surgical procedure. After the animal is adequately anesthetized (see alleviation of pain and distress below), IV lines and EKG monitors will be placed.

A midline abdominal incision will be made and a brief exploration of the abdomen will be performed. A segment of the liver will then be injured with a combination of blunt and sharp trauma so as to cause injury deep into the parenchyma of the tissue. At this point, the (Nd)-YAG laser will be used to obtain hemostasis via a combination of resection and coagulation techniques. After appropriate repair of the liver, similar injuries to the pancreas, spleen, kidney, and intestines will be produced. Each injury will be repaired using the (Nd)-YAG Laser. No more than 50% of the liver parenchyma, or the parenchyma of the other abdominal organs will be injured during the operation. After appropriate hemostasis is obtained, the abdomen will be closed with a standard 3 layer closure, and the animal will be allowed to recover from general anesthesia. The animals will be managed as described below in the post operative care plan.

Each animal will be allowed to recover 1-2 weeks from the initial surgery prior to the second operation. At this surgery the abdomen will be entered in similar fashion and explored. The healing of the liver, pancreas, spleen, kidney, and intestinal repair sites will be assessed by the operating team for the following items: 1 Hemostasis, 2 tissue necrosis, 3 and evidence of any injury to surrounding organs and tissue. After evaluation of the intra-abdominal healing, a similar procedure will be performed on other segments of the above named organs, as described above, and the repair will be made using the (Nd)-YAG laser. At the conclusion of the surgery the animal will then be euthanatized according to the protocol listed below. At no time during the operation or the recovery time will the animal be allowed to suffer, and if appropriate alleviation of pain can not be achieved, the animal will be euthanatized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Investigator failed to respond to requests for annual input.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/70

STATUS: Ongoing

TITLE: Tracheal Reconstruction with Synthetic Gore-Tex Grafts in the Rabbit Model

START DATE: Nov 90

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Miller F. Rhodes, MC; LTC Troy Reyna, MC

KEY WORDS: Tracheal reconstruction, Tracheal prosthesis

Study Objective: To identify a tracheal prosthesis material and surgical technique which may be suitable for reconstruction of the human trachea.

Technical Approach: This study will be conducted in two phases. Phase I will be to determine the maximum graft length allowing successful tracheal reconstruction; Phase II will be designed to determine the minimum interval for subcutaneous implantation required to have successful tracheal reconstruction.

In both Phase I and II the grafts will be implanted in two stages. The first stage will consist of implantation of the Gore-Tex prosthesis in the subcutaneous tissue with a silastic stent to keep the lumen patent and induce fibrous capsule formation. The animals will then be recovered from anesthesia and monitored for a prescribed period of time. The second stage will consist of harvesting the graft, after an appropriate amount of time is allowed for ingrowth of fibrous tissue, and replacing a segment of trachea with the graft. The animals will then be recovered and observed over a period of three weeks time while receiving prophylactic antibiotics.

Initially, two animals will be used to develop the technique and verify suitability of the rabbit as a model. The graft length for these animals will be 1 cm for each rabbit. The graft will remain in the subcutaneous pouch for three weeks prior to the tracheal reconstruction. Three weeks following the tracheal reconstruction, the rabbits will be evaluated to verify patency, infection rates, and degree of re-epithelization in the following manner: The animals will be anesthetized with spontaneous ventilation occurring. Utilizing telescopic bronchoscopy the lumen will be inspected for stenosis. The animal will be euthanatized and the graft cultured and histologically examined for infection and tissue morphology, respectively.

If the outcome of the pilot is successful and the model appears to be appropriate, then the study will proceed as follows:

Phase I: Rabbits will be divided into four groups of six rabbits each:

Group I -3 cm. prosthesis length

Group II -4 cm. prosthesis length

Group III-5 cm. prosthesis length

Group IV -6 cm. prosthesis length

The grafts in these animals will be evaluated at intervals of 4 days, 1 week, 3 weeks, 6 weeks, 9 weeks, and 12 weeks. The evaluation will consist of direct laryngoscopy and bronchoscopy with video recording of the procedure and computer analysis of the dynamic change in lumen size with inspiration and expiration.

Criteria for a failed graft will be 30% obstruction of the resting lumen size or a dynamic decrease to 30% of the lumen diameter with respiratory movement. Brush biopsies of the luminal surface will be taken for bacterial culture and for microscopic evaluation of lumen epithelium.

All surgical and bronchoscopy procedures will be conducted only after animals are appropriately anesthetized as stated below. If unable to prevent animal pain or suffering following procedures, the respective rabbits will be euthanatized according to methods stated below. Any animals that die or are euthanatized prior to the termination of the experiment will be necropsied to determine the cause of death, if applicable, and to evaluate the graft sites grossly and microscopically.

With the exception of 8 long term animals, all remaining animals will be euthanatized 12 weeks following the tracheal reconstruction. The grafts will then be excised and examined grossly and microscopically. Two of the remaining animals from each group will be observed for a total of 6 months to determine if any long term complications occur.

Phase II: After determination of the maximum graft length allowing successful reconstruction, the interval between subcutaneous implantation and transfer of the graft for tracheal reconstruction will be evaluated. On this basis the minimal allowable time between subcutaneous transplantation of the Gore-Tex graft and the tracheal reconstruction can be determined. This will be the final phase of the study as planned. Four groups of six animals each will be required. The graft will be implanted as described in Phase I.

Grafts will be harvested as follows:

Group I -one week

Group II -two weeks

Group III-three weeks

Group IV -four weeks

Following harvesting of the PTFE graft and tracheal reconstruction, each group of animals will undergo evaluation as described in Phase I.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b.(Animal Procedures).

Progress: Investigator failed to respond to requests for annual input.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/27

STATUS: Ongoing

TITLE: . ab Lengthening by Intramedullary Distraction in a Sheep Model; Phase I - Physiologic Feasibility

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: LTC Randolph L. Copeland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Phillip Day, MAJ Phil Holzknecht, CPT Darrell Scales

KEY WORDS: intramedullary distraction, limb lengthening

Study Objective: This testing should demonstrate the feasibility of lengthening a long bone via an intramedullary device in an animal model. The initial phase of the project will be to demonstrate the physiologic potential for adequate new bone to form around an indwelling rod during the process of distraction. Subsequent phases of research would include the practical testing of a prototype indwelling device. Ultimately, a clinical trial in human patients is the goal in the last phases of development.

Technical Approach: This phase of the research will involve the placement of an intramedullary rod into a long bone of the test animals. The rod initially will be interlocked only at one end. Sufficient room will be allowed at either end of the bone to facilitate application of a standard Ilizarov type fixation device. An osteotomy of the bone will be performed at a location well be outside of the isthmus of the bone so as not to be at the site of minimum diameter and maximum reaming damage to the canal. Lengthening will then be performed after a latency period of 7 days. The distraction will be at a rate of 1 mm per day. The goal of lengthening will be 15% of the measured length of the target bone.

The initial study will involve four test subjects. At the end of distraction, two of the animals in the series will continue with the Ilizarov device. The other two animals will have a subsequent completion of the transverse interlocking screws through the intramedullary rod, followed by removal of the external fixator. At the end of 30 days from cessation of lengthening one of the animals from each group will be euthanized and the limb harvested. The other two animals will be processed at 60 days providing there is evidence on radiographs of substantial new bone formation, otherwise delays of 3 week intervals will be added until at least three cortices demonstrate bridging bone on radiographs.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Project delayed due to difficulty in procuring the external fixation equipment. Equipment is now available and animals have been ordered. Tentative date for first surgical procedure is 30 Oct 92. Project will take at least six months from that time depending on success of first procedures and whether the investigators choose to purchase additional external

fixation hardware to allow two animals to be in the fixators simultaneously.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/17

STATUS: Ongoing

TITLE: Early Fracture Dating by Magnetic Resonance Imaging (MRI)

START DATE: Mar 92

ESTIMATED COMPLETION DATE: Jan 94

PRINCIPAL INVESTIGATOR: CPT Darryl Cuda

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ George Momii

KEY WORDS: fracture dating (MRI)

Study Objective: To attempt to accurately date fractures 10 days old or less by MRI

Technical Approach: The initial design will be to study 15 otherwise normal active duty males or females (ages 18-30 years) who will undergo daily T1 and T2 MRI for the first 10 days post fracture. Only fractures of major long bones will be studied for ease of imaging and only two individuals will be studied simultaneously. One radiologist will evaluate all studies.

Progress: One service member enrolled and signed consent but failed to show for appointment.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 90/26

STATUS: Ongoing

TITLE: Artificial Substitutes for the Urinary Bladder in the Porcine Model

START DATE: May 90

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Fernando Diaz-Ball

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Leonard Maldonado, MC; Chief Resident, General Surgery

KEY WORDS: Bladder Substitute, Continent Urinary Diversion

Study Objective: Our objective is to provide training in a variety of techniques previously described in the literature for fashioning a bladder substitute from autologous bowel. Our experience with this will enable us to perform these operations in our patient population. The ongoing nature of the protocol is necessary to maintain technical proficiency and add refinements.

Technical Approach: NOTE: In studies requiring surgery, no surgical procedures will be conducted without the administration of general anesthesia. Anesthesia will be administered and monitored by veterinary staff assigned at Biological Research Service.

The Urology clinic Attending Staff shall devote one or two days each month to performing previously agreed upon continent urinary reservoir procedures. These shall include eg. the Mainz Pouch, the Koch Pouch, and the Indiana Reservoir. (1,2,3)

The common denominator of the various procedures is that autologous bowel is fashioned into a urinary reservoir out of continuity from the fecal stream. This reservoir is then anastomosed to the urethra or to a continent catheterizable stoma.

The proposed model is the porcine. At this time within the training protocol we have elected to euthanize the animals at the end of the surgical procedure prior to recovery from anesthesia. In the future we may choose to request an amendment allowing us to do survival studies as long as animal suffering can be prevented.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: This training protocol is used to review the finer details of technique prior to actual performance of human surgery. Another session will be conducted in preparation for two human radical cystoprostatectomies scheduled for early FY93.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/06

STATUS: Completed

TITLE: Comparison of Cardiopulmonary Responses to Forward and Backward Running

START DATE: Dec 91

ESTIMATED COMPLETION DATE: Jul 92

PRINCIPAL INVESTIGATOR: CPT Timothy Flynn

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Michael Smutok, Dr. R. Jorge Zeballos, Sean Connery, Dr. Idelle Weisman

KEY WORDS: running (forward vs backward)

Study Objective: To compare the cardiopulmonary responses during forward and backward running; to determine if a given running speed forward requires the same oxygen consumption as backward running; to determine if the $\text{VO}_{2\text{max}}$ achieved during forward running can be achieved during backward running; and to determine if a difference in muscle enzymes and lactate buildup exists between forward and backward running.

Technical Approach: Study will include 20 healthy active duty males (18-30y/o). Subjects will be tested over a 2-3 day period. Pulmonary function testing and resting ECGs will be measured on the first day of testing. Also on the first day, a maximal exercise test will be performed on the treadmill for forward running. The maximal exercise test will be an incremental treadmill test lasting approximately 8-12 minutes. Testing will be continuously monitored by ECG and cardiopulmonary measurements as well as by ratings of perceived exertion from the subject. All testing will be stopped at volitional exhaustion and can be stopped by subject by hitting the custom designed button on the treadmill to stop the treadmill. A 2-hour rest period will follow and then 3 submaximal steady state levels treadmill exercise will be performed for 5-10 minutes. The speed of each of these levels will be set after pilot studies have been done to determine the 3 levels to be used. Expected running speeds are 4, 5 and 6 mph and will be the same for all subjects. The order of the 3 submaximal steady state tests will be randomized. On the second day, a maximal incremental exercise test will be performed running backwards in a similar fashion as described above for the forward running testing. A "spotter" will be on hand during all testing who sole responsibility is to steady or catch the subject and/or stop the treadmill during all phases of forward and backward running. A physician will be in the area during all exercise testing. Two venous blood samples will be obtained before and 2 minutes after maximal exercise testing for forward and backward running to measure lactate, CPK and other muscle enzymes. Mean, standard deviation and standard error of the mean will be used to describe each of the variables. Data will be analyzed using the SPSS/PC+ (Chicago II) statistical software program. Two-way analysis of variance with repeated measures will be used to detect significant differences induced by the two conditions (forward and backward running) for each of the tested variables. Significance will be chosen at the 5% level ($P < 0.05$).

Progress: Project complete and manuscript in preparation. Twelve patients participated. Metabolic cost and all cardiopulmonary variables measured were significantly greater for backward locomotion. The increased oxygen consumption required for backward walking/running was almost twice as great as that required for forward locomotion. This fact

has important consequences in being able to provide appropriate exercise prescriptions for both sports conditioning and rehabilitative programs.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/64

STATUS: Ongoing

TITLE: Microvascular Anastomosis of the Rat Femoral Vessels

START DATE: Nov 88

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: MAJ Jeffrey R. Keim

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Microvascular anastomosis

Study Objective: To gain proficiency in microvascular technique so that the technical proficiency gained can be applied to clinical conditions.

Technical Approach: Two survival femoral vessel anastomosis procedures and a third non-survival abdominal vessel surgical procedure will be conducted on each of 40 rats during the training year. At least one staff surgeon will supervise the resident training until they have become proficient. The first procedure (right femoral vessel anastomosis) will be conducted on day 0; the second (left femoral vessel anastomosis) on day 14; and the third (aortic artery anastomosis) will be conducted on day 28 for each respective rat. By the third training day, one of each of these procedures will be done every training period using 3 different rats. The rats will always be euthanatized immediately following completion of the abdominal procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Five animals were used. Study ongoing to compare running versus interrupted microvascular anastomosis. This is an invaluable training protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/18

STATUS: Ongoing

TITLE: Advanced Trauma Life Support Training in the Small Ruminant (Ovine or Caprine Animal Model)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Mark S. Kestner

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Warren F. Bowland

KEY WORDS: ATLS training

Study Objective: This training will enhance the physicians' capabilities of administering advanced trauma life support procedures to patients with emergency medical conditions which require establishment of airways, venous access, and chest and abdominal trauma management.

Technical Approach: The Advanced Trauma Life Support (ATLS) training program is designed for physicians who are not primarily responsible for managing the critically injured patient on a day to day basis. The American College of Surgeons (ACS) Committee on Trauma defines the standards that the ATLS course must adhere to. Initial assessment and management of specific types of injuries are presented to the student through lecture and slide presentations. Students then rotate through practical skill stations associated with the lecture content previously presented. The skill stations and animal lab allow the student to observe and practice to proficiency those life-saving skills necessary in the initial management and stabilization of the trauma patient. The animal lab is a one day affair with one instructor and up to five students assigned to each animal.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: MAJ Kestner assumed PI responsibilities due to MAJ Carey's PCS. No training accomplished during FY92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/01

STATUS: Ongoing

TITLE: The Effect of Fibrin Sealant on Skin Graft Inhibition of Wound Contraction in the Porcine Model

START DATE: Feb 93

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: LTC Michael Kulungowski

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Julio Ortiz

KEY WORDS: Adhesive tissue, Wound healing, Fibrin sealant

Study Objective: Our objective is to determine if fibrin sealant fixation of skin grafts augments their ability to inhibit wound contracture in the porcine model. Theoretically, if the fibrin sealant fixation of skin grafts allows for the inhibition of wound contracture in the animal model, this could be applied to the human patient in a later study.

Technical Approach: Six domestic swine will be utilized. Prior to each surgical procedure, anesthesia will be induced and surgical sites will be prepped. During surgery, four pairs of full thickness skin grafts will be made. A comparison of graft contracture of fibrin sealant treated grafts versus untreated grafts will be made between each pair of wounds. Graft site areas will be quantified every three days postop to day 28 using standardized photography or video digitization into a computer graphics program for analysis. For a period of 48 hours after recovery, the animals will be caged individually and allowed free access to food and water. Afterwards, they will be group housed. Evaluations will not be conducted on wounds showing evidence of infection, excessive hemorrhage or poor coaptations. The surface area of each original graft at day zero will be considered 100% and subsequent determinations will be reported as a percentage of the initial size. Contraction rates of each group will be compared statistically.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Additional funding was requested and approved to allow measurements to be made on the enstronge unit at Texas Tech. When all the equipment and chemicals have been gathered, the protocol will begin. LTC Kulungowski assumed PI duties (Jun 92) due to PCS of CPT Culbertson.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/02

STATUS: Ongoing

TITLE: The Effect of Fibrin Sealant on Breaking Strength of Incisional Wounds in the Porcine Model

START DATE: Feb 93

ESTIMATED COMPLETION DATE: Oct 93

PRINCIPAL INVESTIGATOR: LTC Michael Kulungowski

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Julio E. Ortiz; LTC Phillip L. Day

KEY WORDS: Fibrin sealant

Study Objective: To determine if fibrin sealant enhances wound healing as evaluated by wound breaking strength and histological evaluation of tissue in the animal model (i.e., fibroblast proliferation, angiogenesis, etc.). Should fibrin sealant prove efficacious in the animal model to promote wound healing, this could be utilized in the human patient in a comparative study to evaluate wound healing and thus promote the strength of the wound.

Technical Approach: Six domestic swine will be utilized. Prior to each surgical procedure, anesthesia will be induced and surgical sites will be prepped. During the initial surgery, four pairs of surgical incisions will be made. A comparison of fibrin sealant versus normal healing will be made between each pair of wounds. One pair of wounds will be harvested from each animal at day 7, 14, 21, and 28 post wounding. Breaking strengths and histological analysis of paired wounds will be determined. For a period of 48 hours after recovery, the animals will be caged individually and allowed free access to food and water. Afterwards, they will be housed together. Evaluations will not be conducted on wounds showing evidence of infection, excessive hemorrhage or poor coaptations. Adhesiveness of each group will be compared statistically.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Additional funding has been requested and approved to allow measurements to be made on the enstronge unit at Texas Tech. Once all the equipment and chemicals have been acquired, the protocol will begin. LTC Kulungowski assumed PI duties (Jun 92) due to PCS of CPT Culbertson.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/11

STATUS: Ongoing

TITLE: General Surgery Department Vascular Surgery Training Program Utilizing the Porcine Model

START DATE: Jan 91

ESTIMATED COMPLETION DATE: Indef

PRINCIPAL INVESTIGATOR: MAJ Carl G. Lauer

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Vascular surgery training

Study Objective: This training is designed to teach General Surgery resident physicians the basic operative skills required to perform vascular surgery.

Technical Approach: The exercise will concentrate on developing the surgeon's ability and confidence in handling vascular tissues, sutures, and prosthetics. Survival and non-survival procedures will be performed on each animal.

(1) The first animal will undergo transection and primary re-anastomosis of the aorta and vena cava. It will be recovered for 7 to 14 days, then undergo placement of a peripheral (femoral) PTFE A-V fistula. The abdomen will be re-explored, and the original aortic and vena caval anastomosis will be examined. The animal will then be euthanatized while the animal is still under anesthesia.

(2) The second animal will undergo placement of an interposition Dacron sleeve graft of the aorta. It will be recovered, and in 7 to 14 days it will undergo formation of bilateral femoral Brescia fistulae. The abdomen will then be re-explored, and the aortic graft examined. The animal will then be euthanatized.

(3) The third animal will undergo placement of a peripheral (femoral) PTFE A-V fistula. It will then undergo laparotomy and formation of a portocaval shunt. It will then be euthanatized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: MAJ Lauer assumed PI responsibilities due to LTC Runke's PCS. Four pigs were utilized during FY92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/46

STATUS: Ongoing

TITLE: Familial Hirschsprung's Disease: Study of a Texas Cohort

START DATE: Apr 92

ESTIMATED COMPLETION DATE: Nov 92

PRINCIPAL INVESTIGATOR: LTC Troy M. Reyna

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Hirschsprung's Disease

Study Objective: To increase the awareness of the pediatric community of the occurrence of sporadic familial Hirschsprung's.

Technical Approach: A case report of a seven-week old male infant will be presented with constipation secondary to Hirschsprung's upon workup and evaluation. Study will include his relation to the cohort mentioned above which spans four generations and includes six proven/suspected cases of Hirschsprung's.

Progress: Six family members were studied. Investigator awaiting additional information on other family members of the family tree in order to determine type of mendelian or non-mendelian inheritance.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/54

STATUS: Ongoing

TITLE: Evolutionary Trends and Results of Cholecystectomy Laparoscopic versus Open in a Residency Teaching Program

START DATE: May 92

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: LTC Troy M. Reyna

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Francis Tapia

KEY WORDS: cholecystectomy

Study Objective: To document changing trends in the training of residents in the treatment of gallbladder disease and the safety and efficacy of these techniques.

Technical Approach: A retrospective evaluation of this institution's results with laparoscopic cholecystectomy will be studied. Cases will be evaluated upon the level of expertise of both attending surgeon and the resident performing the case with regard to operative results and complications. A learning curve will thus be constructed and trends assessed to best determine the optimal implementation of this new surgical technique in a surgical training program.

Progress: One hundred forty-two procedures reviewed. Investigator cataloging additional patient charts/cases in order to attain number of significant patients.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/55

STATUS: Ongoing

TITLE: Spectrum of Colorectal Injuries in Children: A Ten Year Review

START DATE: Aug 92

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: LTC Troy M. Reyna

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Barry Hammacker

KEY WORDS: colorectal injuries

Study Objective: To document changing trends in the management of colorectal injuries in pediatric patients when contrasted with adult techniques and to assess any trends in evolution of techniques over the last decade of advancing trauma management. Also noted will be the differences in epidemiology between adult and pediatric injuries to this organ.

Technical Approach: A retrospective clinical evaluation of all records of pediatric patients admitted to CONUS medical facilities for the last ten years with a diagnosis of colorectal injuries will be undertaken. Charts will be collected, blinded with analysis of data from the admission physical exam, operative report(s), narrative summary, and autopsy report, if applicable.

Progress: Investigator just recently received 21 of 23 patient charts and is now ready to analyze data. The other two charts were not available.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/09

STATUS: Terminated

TITLE: A Multicenter, Double-blind, Randomized, Comparative Study of the Efficacy and Safety of Intravenous Temafloxacin versus Imipenem-Cilastatin Sodium in the Treatment of Intra-abdominal Infection (Monitor: MAJ David Slagle)

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Jul 92

PRINCIPAL INVESTIGATOR: LTC Lawrence Runke

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Anthony Canfield

KEY WORDS: Temafloxacin

Study Objective: Temafloxacin is a fluoroquinolone that has a broad spectrum of antimicrobial activity in vitro, and appears to have more anaerobic and gram negative coverage than other quinolones. This double-blind, randomized study is designed to determine the in vivo efficacy and safety of Temafloxacin in comparison with Imipenem-Cilastatin, in patients with intra-abdominal infections.

Technical Approach: This study is a randomized, double-blind multicenter study in which patients who meet the inclusion criteria will be randomly assigned to either of two groups. One group will receive Temafloxacin 800 mg IV q12, the other group will receive Imipenem-Cilastatin Sodium 500 mg IV Q6 hours. Efficacy will be assessed by microbiologic findings and by evaluation of clinical signs and symptoms of infection. Safety evaluations will consist of periodic laboratory tests and physical examinations. The patients will be monitored for evidence of drug intolerance and for the development of clinical and/or laboratory evidence of adverse events.

Semiannual Review: Apr 92

Progress: Project terminated 10 Jun 92 because of adverse consequences related to its use; none occurred at WBAMC.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/44

STATUS: Terminated

TITLE: Determination of Bone Manganese Levels in Patients with Chondromalacia Patella.
(Monitor: COL Maldonado)

START DATE: May 88

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ John Cook, MC; MAJ John Uhorchak

KEY WORDS: Chondromalacia, Manganese

Study Objective:

1. Identify and characterize by symptoms and physical findings the patient group with patellofemoral pain syndrome.
2. When performing diagnostic arthroscopy of patients with knee impairments, observe and record the character of the patellofemoral articular cartilage including objective measurement of cartilage softness.
3. Obtain 1 gram bone biopsy specimens from the distal femoral metaphysis at the time of arthroscopy and determine manganese content of bone mineral.
4. Perform multivariate analysis of data to observe possible correlations of bone manganese levels with severity of signs and symptoms of chondromalacia, cartilage appearance and measure cartilage softness.

Technical Approach: The study will be conducted at WBAMC and UTEP. Clinical evaluation will take place at WBAMC. The patients presenting to the Orthopaedic Clinic with knee disorders requiring arthroscopy or arthrotomy will be counseled and asked to volunteer for this study. If their informed consent is obtained they will be asked to provide information to complete the clinical questionnaire. The results of a comprehensive physical examination of the knees will also be recorded. At arthroscopy or arthrotomy the character of the articular cartilage will be noted and graded for severity of chondromalacia by the criteria of Hugston, et al. The indentation hardness of the cartilage will then be measured by a modification of the Brinell hardness measurement technique. This will be done with a locally fabricated instrument which can be autoclave sterilized. A biopsy specimen consisting of 1 gram of bone will be obtained from the distal femoral metaphysis using standard bone biopsy techniques. A portion of the specimen will be submitted for routine histology and the remainder will be analyzed for manganese content. The portion for manganese assay will be asked at 900 degrees centigrade, the ash weighed, dissolved in EDTA decalcifying solution, and analyzed with a Beckman plasma spectrophotometer at UTEP. All biopsy specimens sent to UTEP will be identified by code number only.

Progress: Project terminated on semiannual review (Apr 92) due to PCS of key personnel.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/25

STATUS: Ongoing

TITLE: Vascular Changes Associated with Stress Reaction of Bone in the Rat

START DATE: May 89

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ John M. Uhorchak, MC

KEY WORDS: Stress reaction, bone

Study Objective: To determine the sequence and character of vascular changes which occur in living bone after it has been subjected to repeated physical stress.

Technical Approach: We will study the character and chronological sequence of vascular changes which occur in rat legs subjected to mechanical stress in the absence of confounding electrical shocks.

a. Thirty anesthetized rats will have their left leg cyclicly mechanically stressed using the techniques of Scully et.al. The tibias will be cyclicly strained to 0.5 mm by repeated application of a 3 point bending load. 10,000 cycles of strain will be applied to the left tibia of each rat at a rate of 10 Hz. The animals will then be recovered from anesthesia and maintained in standard laboratory cages with unrestricted activity, on a standard laboratory diet. Groups of 2 animals will be selected at random on days 0, 1, 2, 3, 4, 5, 6, 7, 10, 12, 15, 18, 24 and 30 days after the initial strain loading.

b. On the date selected the animals will be anesthetized with Nembutal at a dose of 25mg/kg intravenously. The rats will then be heparinized and injected with Xylocaine to prevent vascular thrombosis and to ensure maximum vasodilation. The animals will then be given a lethal dose of Nembutal. After euthanasia the abdomens will be opened through a midline abdominal incision. The aorta and inferior vena cava will be transected and cannulated. Using techniques prescribed in the Microfil product literature the aorta and both lower extremities will be perfused with Microfil at a pressure of 150 mm of mercury. Perfusion will continue until the flow of the Microfil is returned via the inferior vena cava. At that point the animals will be refrigerated to allow overnight curing of the Microfil. As each animal has had only one leg stressed, the contralateral leg will serve as a control. Radiographs will be taken of both lower extremities to delineate the microvascular structure. Microfil is a radio-opaque material. After the radiographs are obtained, tissue clearing will be performed by the following technique: on the first day both tibias will be immersed in a 25% ethanol solution. On the second day 50% ethanol, on the third 75% ethanol, on the fourth day 95% ethanol and on the fifth day a new solution of absolute alcohol. On the sixth day the specimen will be immersed for 24 hours in methylsalicylate. If the tissue is not clear it will be returned to a 95 % ethanol solution and the fine cleaning procedure steps will be repeated. Photographs will then be taken of the vascular tree which will have been filled with colored Microfil. The tibias will then be imbedded and sectioned for standard histologic sectioning.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or

anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: All activity on this project was halted during Operation Desert Storm and has only recently been resumed. All specimens were preserved and are in excellent condition. Specimens are being examined by microradiography and being prepared for serial histological studies. Techniques for embedding the cleared rat legs in plastic to permit serial sectioning are slowly being perfected. No animals used in FY92.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/07

STATUS: Terminated

TITLE: The Timing Principle: A comparison of vecuronium versus atracurium for rapid sequence induction of anesthesia

START DATE: Jan 91

ESTIMATED COMPLETION DATE: Apr 92

PRINCIPAL INVESTIGATOR: MAJ Sanford Silverman

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC S. Ciresi; MAJ C. Hauser; CPT V. Cassani

KEY WORDS: Vecuronium, Atracurium, Anesthesia

Study Objective: To compare intubating conditions with atracurium utilizing the timing principle.

Technical Approach: In an effort to define the effectiveness of these techniques, a prospective study will be undertaken to compare the timing technique to that of rapid sequence induction with succinylcholine. The study will utilize state-of-the-art monitoring and routine dosages of anesthetic agents. A comparison will be made as to whether atracurium is as reliable as vecuronium utilizing the timing technique.

Progress: Study was terminated for several reasons. The associate investigator PCS'd and LTC Hauser, the new Phase II Nurse Anesthesia Course Director, no longer feels this research project is needed for training CRNA students and no longer has the staffing to conduct clinical research. A total of twelve subjects were studied with no adverse outcome.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/66

STATUS: Completed

TITLE: Logistics of Surgery and Modern Warfare: Epidemiologic Review of the Lessons Learned in "Desert Storm" during Duty with a Combat Support Hospital

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: MAJ William C. Sippo

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Combat Support Hospital (ODS)

Study Objective: To define the modern military medical requirements for rapid mobilization, deployment, combat and aftermath of modern warfare with emphasis on improving future operations.

Technical Approach: Retrospective review of inpatient and outpatient records of patients treated during the operational period of the 18th Combat Support Hospital in Southwest Asia (Sep90-Mar 91).

Progress: Project completed and presented to the Clinical Congress of the American College of Surgeons (Oct 91) and at the Association of Military Surgeons 5th Annual Combat Trauma Symposium in Norfolk, VA (Jun 92).

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/82

STATUS: Terminated

TITLE: Ultrasound Screening for AAA in Asymptomatic Males Over Age 55

START DATE: Sep 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT James B. Smith

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhail III, MC; CPT Donna Corvette, MC; MAJ Cass Conaway, MC; LTC James C. Griffith, MC

KEY WORDS: AAA, Ultrasound Screening

Study Objective: To ascertain the incidence of AAA (Abdominal Aortic Aneurysm) in asymptomatic males over age 55 admitted to WBAMC for other reasons.

Technical Approach: All males age 55 and older admitted to Internal Medicine or Department of Surgery wards at WBAMC will be included in the study (approximately 180 per month) and will receive an abdominal aortic ultrasound examination. Patients with prior abdominal aortic surgery for aneurysm or occlusive disease will be excluded. All participants will be provided with a written explanation of the protocol. Patients with known AAA previously proven by ultrasound or CT Scan need not be submitted to repeat examination, if last previous study was within the past 6 months. Patients will be notified of the results of the ultrasound examination. Patients with positive findings for AAA will be referred to Vascular Surgery Service for appropriate follow-up. A negative finding will result in completion of participation in the study. The study will run for six months.

Success/failure criteria: Aneurysm will be defined as enlargement of the anteroposterior or transverse aortic diameter more than 1.5 times the diameter of the proximal aorta, or greater than 4 centimeters in diameter.

Data Collection: Patients will be interviewed by a physician for pertinent history of smoking, HTN, CAD, ASPVD, hyperlipidemia, or family history of AAA (maternal versus paternal).

Ultrasound examination will be performed by the Department of Radiology using their standard real-time ultrasound equipment: Diasonics model DRF 400, and read by a staff radiologist.

Progress: Project terminated due to critical shortage of ultrasound technologists now and in the foreseeable future.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/12

STATUS: Completed

TITLE: Determination of Percutaneous Inoculum Size for Cannulated Needle, Suture Needle and Scalpel Using a Porcine Model

START DATE: Feb 91

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Walker A. Wynkoop

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Al Landry

KEY WORDS: Inoculum size determination

Study Objective: The purpose of this study is to quantitatively measure:

- (1) The percutaneous blood inoculum (PBI) size for cannulated needles, suture needles, and scalpels.
- (2) The relative blood inoculum size reduction by simple incision and debridement.
- (3) To use the above information to make recommendations for emergent active treatment of high risk inocula by type of injury.

Technical Approach: The study will be conducted in the Nuclear Medicine Service facilities at WBAMC. Frozen, unpreserved porcine cadaver feet harvested from euthanatized animals from other studies will be thawed to room temperature. Small amounts of investigator's blood will be mixed with technetium using standard nuclear pharmacy safety precautions in the WBAMC Nuclear Pharmacy. This facility is a federally licensed nuclear materials user; license # 42-05255-07. This blood will be used to create PBI by scalpel, suture needle, and cannulated needle. Inocula size will be measured before and after simple I+D.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Amendment: Study design and labeling techniques were refined to provide better data for publication.

Progress: Project completed Jun 92. A total of 98 feet were used in the study. The data shows that the PCI volume for a scalpel or cannulated needle are about the same, and the PCI volume of a suture is less than 1/10 the size. A cannulated needle with injection mechanism has a PCI approximately fourteen times larger than that of the scalpel or cannulated needle without injection mechanism. Application of the CDC infection rate for a PCI is inappropriate when referring to the PCI obtained in the operating suite and will lead to a falsely high risk of acquiring HIV infection. Recommendations for emergent treatment of PCI from high risk patient are: Follow PHS recommendation; Suture PCI (wash outer skin - no I+D); Scalpel PCI (wash outer skin immediately, irrigate wound with lidocaine, open laceration with hemostate and irrigate with >120ml NS); Cannulated Needle PCI without injection mechanism (wash outer

skin immediately, consider I+D especially if patient has advanced HIV infection); **Cannulated Needle PCI with injection mechanism** (wash outer skin immediately, do emergent 15-30 I+D). Two separate articles were presented; one at the 8th Annual Residents & Fellows Conference, Southern Orthopedic Association (Nov 91, Atlanta, GA) and the other at the 85th Annual Scientific Assembly, Southern Medical Association (Nov 91, Atlanta, GA)

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 91/16

STATUS: Terminated

TITLE: Evaluation of Emergency Active Management of Accidental Exposure to Allogenic Whole Blood for Orthopedic Type Injuries in the Porcine Model

START DATE: Mar 91

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Walker A. Wynkoop

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Albert Moreno

KEY WORDS: Needlestick, HIV inoculum size

Study Objective: The purpose of this study is to evaluate:

- (1) The relative percutaneous blood-inoculum (PBI) size for cannulated needles, power driven smooth and threaded K-wires, and power driven twist drills.
- (2) The migratory behavior of the allogenic blood inoculum over time.
- (3) The efficacy of incision and debridement (I+D) in reducing the allogenic blood inoculum size.
- (4) The relative allogenic blood inoculum size reduction by I+D as a function time.
- (5) To use the above information to make recommendations for emergent active treatment of high risk inocula by type of injury, including a recommended time of efficacy.

Technical Approach: This study is to be an animal model study using juvenile porcine swine. One swine will model a "high risk" patient. It will have it's whole blood tagged with technetium. Another swine will model an "ortho staff" member of an orthopedic surgical team. This "ortho staff" swine will then be inoculated with allogenic blood from the "high risk" swine using protocols modeling an accidental percutaneous blood inoculation.

The study will be conducted in five one-day sessions (with provision for a 6th make-up session). A total of 10 swine will be utilized. Each session will be limited to one type of accidental orthopedic percutaneous inoculation.

Sharp instruments in the orthopedic OR suite cause PBI in various ways. The most dangerous are those that carry a large whole blood inoculum. This study will look at several accidents that can happen during open reduction and internal fixation of bone fractures. Power tool use during palpation of a bone fragment is often the best way to fixate a bone without added soft tissue stripping. This method runs the risk of causing a PBI by a power tool that has just traversed soft tissue and bone.

In order to model these injuries in vivo, two swine under general anesthetic will participate as the "high risk patient" and the "ortho staff". Accident mechanisms to be study are phlebotomy needlestick held by syringe plunger; phlebotomy needlestick held by syringe body; power driven twist drill; power driver smooth K-wire; and power driven threaded K-wire. The following variables will be measured for each accidental mechanism:

- 1) The effect of time on inoculum size. Will the allogenic blood migrate from the injury site over time?
- 2) The effect of immediate, limited I&D on inoculum size.
- 3) The effect of delayed, limited I&D on inoculum size.

Nuclear scanning will be used for determination of inoculum size with counts time-adjusted for decay. Scans will be taken at each step of the procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Project terminated Jun 92. Needlestick in the feet of anesthetized swine demonstrated redistribution and efficacy of I+D in reducing redistribution of tagged whole blood. The study was not completed because the gamma camera in the Biological Research Service is not accurate enough for such small samples and adequate concentrations of whole body technetium were not possible within safety standards to provide a higher count in the twist drill transfer from donor to recipient.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 88/52

STATUS: Ongoing

TITLE: Combat Trauma Life Support Procedure in the Sheep Model

START DATE: Oct 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: 2LT J. Walls

DEPARTMENT: FBT

FACILITY: 3ACR, Ft. Bliss, TX

ASSOCIATED INVESTIGATORS: WO1 Abelardo Montes, PA

KEY WORDS: Life support, Combat trauma

Study Objective: To train Physicians Assistants and Line Medics who are not dealing with major trauma on a day-to-day basis, but may be called upon to perform this function in a combat environment. The sheep model will simulate human trauma.

Technical Approach: Animal procedures include:

1. Cricothyroidotomy
2. Venous Cutdown
3. Intubation
4. Chest Trauma Management
 - a. Needle decompression
 - b. Tube thoracostomy

ATLS training manuals will be used for each training procedure.

Progress: CW2 Harvey PCS'd. New PI is 2LT Walls. MAJ Harris (DCI vet) and LT Walls have reviewed this protocol and assess it as an important training project for physician assistants and line medics. Maximum and efficient use of each animal model was adhered to during the procedures.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 92/11

STATUS: Ongoing

TITLE: Emergency Life Support Training for Combat Medics in the Small Ruminant (Ovine or Caprine) Animal Model

START DATE: Jan 92

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: 2LT J. Walls

DEPARTMENT: FBT

FACILITY: 3ACR, Ft. Bliss, TX

ASSOCIATED INVESTIGATORS:

KEY WORDS: life support training

Study Objective: This training will enhance the combat medical aidman's (Medic's) capabilities of administering emergency lifesaving procedures to patients with emergency medical conditions which require establishment of airways, venous access, and chest trauma management.

Technical Approach: The emergency life support training program is designed for medics who are responsible for providing first to third echelon care to the critically injured patient (echelon 1- self & buddy aid; echelon 2- combat lifesaver; echelon 3- medical specialist). Procedures taught will be according to the American College of Surgeons (ACS) Committee's Advanced Trauma Life Support Course. Initial assessment and management of specific types of injuries are presented to the student through lecture and slide presentations and a written examination. Students who successfully complete lecture and examination requirements, then rotate through animal laboratories associated with the lecture content previously presented. The animal laboratory allows the student to observe and practice to proficiency those life-saving skills necessary in the initial management and stabilization of the trauma patient. The animal laboratory is approximately 2-3 hours per cycle. Each animal station will consist of one instructor and no more than four to five students.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Seven sheep were used during FY92. This protocol has provided extremely valuable training for medical personnel of a deployable, combat-ready unit. Each trainee benefited from hands-on training in techniques essential to save lives on the battle field. Maximum and efficient use of each animal model was adhered to during the procedures. Critiques following the procedures by the trainees and associate instructors have been extremely positive.

DETAIL SUMMARY SHEET

DATE: 1 October 92

PROTOCOL #: 89/42

STATUS: Ongoing

TITLE: The Utility of Thermographic Evaluation in the Diagnosis of Lower Extremity Injuries During Army Initial Entry Training

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC Bruce H. Jones

DEPARTMENT: USAREM

FACILITY: TRADOC

ASSOCIATED INVESTIGATORS: Dr. Murray Hamlet, DVM; COL (Ret) Margarete Di Benedetto

KEY WORDS: Thermogram (graphic), Scintigraphic

Study Objective:

1. To document the sensitivity and specificity of thermography to detect the presence or absence of injuries in general compared to clinical standards and more specifically to:

(a) To document the specificity and sensitivity of thermography in the diagnosis of stress fractures verses bone scans and x-rays as the diagnostic standard. Also, to calculate the positive and negative predictive value of thermography in the diagnosis of stress fractures based on the prevalence of stress observed in this and other epidemiologic studies.

(b) To document the sensitivity and specificity of thermography to detect injuries other than stress fractures verses the level of certainty of clinical diagnosis, i.e., the presence or absence of observable signs and the number of positive signs such as swelling, erythema, ecchymosis, point tenderness, decreased range of motion, etc. for a particular diagnosis. Also, to document the sensitivity and specificity of thermography verses the degree of severity of injury measured in days of limited duty or hospitalization. Also, positive and negative predictive value will be assessed once the prevalence of specific injuries in the cohort are established. (As an aside, the potential for paradoxically decreased sensitivity of thermography when such soft clinical standards are used is recognized, however, the use of two or more operationally defined clinical standards, i.e., level of clinical certainty and degree of severity of the diagnosis should help to recognize a paradox when it arises.

2. To qualitatively and quantitatively describe the thermographic patterns for specific injuries if they are perceived to exist.

3. To determine whether the thermographic patterns "normalize" as injuries heal in a way that would assist in making decisions regarding return of soldiers to duty.

4. To determine whether individuals with flat feet or high arches are likely to suffer more injuries to the lower extremities than those with "normal" feet. Also, to determine whether the thermograms of individuals with flat feet or those with high arches are more likely to be positive (indicating "chronic stress") than individuals with "normal" feet at baseline (prior to onset of basic training) and episodically during basic training.

5. To determine the effect of training volume (running and marching mileage) on the incidence of injuries and on the qualitative and quantitative patterns of lower extremity thermograms.

6. To determine whether the thermographic patterns observed are more likely to be positive for sub-populations grouped on the basis of age, race, body composition, past activity, and physical fitness.

7. To determine the incidence of commonly occurring training-related injuries and the amount of morbidity (days of limited duty, etc.) associated with each. With these data estimates of the impact of early diagnosis and appropriate return to duty through use of thermography will be made.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Project terminated. PI PCS'd and did not reply to request for annual input.

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